NUCLEOPHILIC ADDITIONS TO DIBENZOYLACETYLENE AND RELATED STUDIES

A Thesis Submitted
in Partial Fulfilment of the Requirements
for the Degree of
DOCTOR OF PHILOSOPHY

By
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to the
DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY, KANPUR
JULY, 1981

TO

MY GRANDMOTHER

AND

PARENTS

DEPARTMENT OF CHEMISTRY

Indian Institute of Technology, Kanpur, India

CERTIFICATE I

This is to certify that Mr. P. M. Scaria has satisfactorily completed all the courses required for the Ph.D. degree programme. These courses include:

Chm 500	Mathematics for Chemists I
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Chm 521	Chemical Binding
Chm 523	Chemical Thermodynamics
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Chm 800	General Seminars
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Chm 900	Graduate Research

Mr. P. M. Scaria successfully completed his Ph.D. Qualifying Examination in January 1977.

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Certified that the work embodied in this thesis entitled: "NUCLEOPHILIC ADDITIONS TO DIBENZOYLACETYLENE AND RELATED STUDIES" has been carried out by Mr. P. M. Scaria under my supervision and the same has not been submitted elsewhere for a degree.

M. V. GEORGE
Thesis Supervisor

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India, under the supervision of Professor M. V. George.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

P. M. Scaria

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P. M. Scaria

CONTENTS

PREFACE

The thesis entitled: "Nucleophilic Additions to Dibenzoylacetylene and Related Studies" is divided into four chapters. Chapter 1 deals with a brief survey of some aspects of the nucleophilic additions to acetylenic ketones. Some of the nucleophiles of particular interest include, amines, hydroxy compounds, hydrazones and related systems.

Chapter 2 of this thesis describes the results of our studies on the nucleophilic additions of some of the representative examples of nitrogen containing nucleophiles such as hydrazides, phenylhydrazides, hydrazones, phenylhydrazones and related substrates to dibenzoylacetylene (DBA). The reaction of benzoylhydrazine (1) with DBA in tetrahydrofuran (THF) at room temperature, for example, gave a 92% yield of 2-(2'-benzoylhydrazono)-1,4-diphenylbutan-1,2,4-trione (2). Treatment of 2 with either HCl in methanol or with orthophosphoric acid gave a nearly quantitative yield (~95%) of 5-benzoyl-3-phenylpyrazole (3). Similarly, the reaction of benzoylphenylhydrazine (4) with DBA in methanol gave a 89% yield of 2-(2'-benzoyl-1'-phenylhydrazo)-1,4-diphenylbut-2-ene-1,4-dione (5). An attempted cyclization of 5 by treatment with orthophosphoric acid gave a 80% yield of 5-benzoyl-1,3-diphenylpyrazole (6), along with a 70% yield of benzoic acid. The reaction of ethyl N,C-diphenylglycinate (7) with DBA, on the other hand, gave a 90% yield of

2,3-dibenzoyl-4-hydroxy-1,5-diphenylpyrrole (8).

In continuation of our studies, we have examined the reactions of a few hydrazones such as benzaldehyde hydrazone (9), benzophenone hydrazone (10) benzaldehyde phenylhydrazone (11) and p-anisaldehyde phenylhydrazone (12) with DBA. The reaction of 9 with DBA in methanol, for example, gave a 1:1 adduct, 2-(1'-hydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (13, 88%), whereas 10, under analogous conditions gave a 93% yield of 2-(1'-hydrazinyl-2'-benzhydrylidene)-1,4-diphenylbut-2-ene-1,4-dione (14). The reaction of 11 with DBA, on the other hand, gave a mixture of products consisting of 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (15, 19%) and 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (16, 8%). Similar results have been obtained in the reaction of 12 with DBA. The reaction of benzil monohydrazone (17) with DBA in refluxing xylene, on the other hand, gave a 91% yield of 3,4-dibenzoyl-5,6-diphenylpyridazine (18). Treatment of 18 with hydrazine resulted in the formation of 3,4,5,8-tetraphenylpyridazino[4,5-c]pyridazine (19, 68%).

The reaction of a diamine nucleophile such as ethylenediamine (20) with DBA has been shown to give a mixture of products consisting of 2-(2'-oxo-2'-phenylethylidene)-3-phenyl-1,2,5,6-tetrahydropyrazine (21, 69%) and N,N'-bis-(2'-(1',4'-diphenylbut-2'-ene-1',4'-dione))-1,2-diaminoethane (22, 31%). Reasonable

mechanisms have been suggested to account for the formation of the different products in these reactions.

Chapter 3 of this thesis deals with the reactions of a few ortho-functionalized phenol and aniline derivatives with DBA. The reaction of salicylaldehyde (23) with DBA, for example, has been shown to give different products depending on the reaction conditions. Treatment of an equimolar mixture of 23 and DBA in acetone in the presence of potassium carbonate at room temperature, for example, gave a 68% yield of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (24), whereas in refluxing acetone, under analogous conditions, a 58% yield of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (25) was obtained. The structures of 24 and 25 have been established on the basis of analytical data, spectral information and chemical evidences. It has been observed that 24 is converted to 25, in the presence of acids or on heating, whereas both 24 and 25 are converted to the same methoxy derivative, 2,3-dibenzoyl-2-methoxy-2H-1-benzopyran (27), on treatment with concentrated sulfuric acid in methanol. It has been inferred on the basis of UV studies and other supporting evidences that both 24 and 25 are converted to the same benzopyrylium cation 26, under acidic conditions, which then leads to 27, in presence of methanol or reverts back to 25, on reaction with water. Similarly, the reaction of o-hydroxyacetophenone (28)

with DBA has been shown to give a 62% yield of 2,3-dibenzoyl-4-methyl-4H-1-benzopyran-4-ol (29).

Some of the ortho-carbonyl substituted anilines that we have studied include anthranilamide (30), anthranilic acid (31) and ethyl anthranilate (32). The reaction of 30-32 with DBA gave, in each case, the corresponding 1:1 adducts, namely, 1,4-diphenyl-2-(N-2-carboxamidophenylamino)but-2-ene-1,4-dione (33, 89%), 1,4-diphenyl-2-(N-2-carboxyphenylamino)but-2-ene-1,4-dione (34, 88%) and 1,4-diphenyl-2-(N-2-ethoxycarbonylphenylamino)but-2-ene-1,4-dione (35, 70%). Our attempts to cyclize 34 and 35 under acid-catalysed conditions were unsuccessful and resulted in the formation of cleavage products such as anthranilic acid (31) and 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (16). Reasonable mechanisms have been suggested to account for the formation of the various products in these reactions.

The results of our studies on the photochemical transformations of a few enamine diones and related systems form the subject matter of Chapter 4 of this thesis. Photochemical transformations of a few enamine diones such as 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (36), 1,4-diphenyl-2-(N-methyl-N-phenylamino)but-2-ene-1,4-dione (37) and 1,4-diphenyl-2-piperidinobut-2-ene-1,4-dione (38) have been attempted. Irradiation of 36 in methanol, for example, either

in a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) or employing a 450-W Hanovia medium-pressure mercury lamp, led to the recovery of the starting material. Similarly, enamine diones carrying a cis-1,2-dibenzoylalkene chromophore, such as 37 and 38 did not undergo any appreciable change, on irradiation. Attempts to prepare the N-benzoyl and N-acetyl derivatives of enamine diones such as 36 resulted in the formation of the corresponding enol esters. Thus, benzoylation of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (36) gave a 78% yield of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (39), whereas acetylation of 36, under analogous conditions gave a 76% yield of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (40). Similarly, the benzoylation of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (41) gave a 60% yield of 4-benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one (42).

Irradiation of the enol benzoate 39, using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a mixture of products consisting of 1,4-diphenyl-4-methoxy-2-(N-phenylimino)but-3-en-1-one (43, 75%) and benzoic acid (65%). It was shown in a separate experiment, that the mere refluxing of 39 in methanol also gives rise to the enol ether 43 (70%). In contrast, the irradiation of a solution of 39 in methanol using a 450-W Hanovia medium-pressure mercury lamp gave a mixture of

products consisting of the enamine dione (36, 40%), 1,4-diphenyl-3-methoxy-2-(N-phenylamino)but-2-ene-1,4-dione (44, 19%) and benzoic acid (50%). On the other hand, irradiation of a benzene solution of 39, under analogous conditions, gave a mixture of 36 (61%) and benzoic acid (24%).

Irradiation of a methanol solution of the enol acetate 40, using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a 60% yield of the enol ether 43, whereas the irradiation of 40 using a 450-W Hanovia medium-pressure mercury lamp gave a 34% yield of the deacetylated product 36. In contrast, the irradiation of a benzene solution of 40 did not result in any photoconversion. Similarly, the irradiation of a methanol solution of the enol benzoate 42, using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a mixture of the enamine dione 41 (76%) and benzoic acid (83%). Likewise, the irradiation of 42 in methanol using a 450-W Hanovia medium-pressure mercury lamp gave a mixture of 41 (73%) and benzoic acid (51%).

In continuation of our studies, we have examined the photochemical transformations of some enehydrazine diones such as 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (15) and 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (45). Irradiation of

a solution of 15 in methanol, using a 450-W Hanovia medium-pressure mercury lamp gave a 63% yield of 4,5-dibenzoyl-1,3-diphenylpyrazole (46), whereas irradiation of 15 in benzene, under analogous conditions, gave a 77% yield of 46. Similarly, the irradiation of 45 in methanol gave a 33% yield of 3-(p-anisyl)-4,5-dibenzoyl-1-phenylpyrazole (47). Reasonable mechanisms have been suggested to account for the formation of the different products in the phototransformations of 39, 40, 42, 15 and 45.

CHAPTER I

NUCLEOPHILIC ADDITIONS TO ACETYLENIC KETONES - A BRIEF SURVEY

I.1 INTRODUCTION

Several types of addition reactions involving acetylenic ketones are reported in the literature. Acetylenic ketones function as dienophiles in Diels-Alder type of reactions, as dipolarophiles in 1,3-dipolar cycloadditions and also react with several nucleophiles, giving rise to a variety of products.[1]

Nucleophiles, in general, add to acetylenic ketones giving rise to dipolar intermediates, which undergo further transformation, depending upon the reaction conditions, the nature of the nucleophile and also the substituents in the acetylenic ketones. Some of these reactions have been successfully employed in the synthesis of several interesting heterocycles. The high reactivity of acetylenic ketones, particularly towards nucleophiles is attributed to the facile polarisation of the carbon-carbon triple bond, due to the electron-accepting carbonyl group(s), conjugated with it.

A brief survey of some of the nucleophilic additions to acetylenic ketones and the subsequent transformations of the adducts formed, is presented in this chapter.

I.2 NITROGEN CONTAINING NUCLEOPHILES

I.2.1 Primary Amines

Aliphatic primary amines readily react with acetylenic ketones, yielding simple 1:1 adducts consisting of α,β-unsaturated β-aminoketones.[2-28]

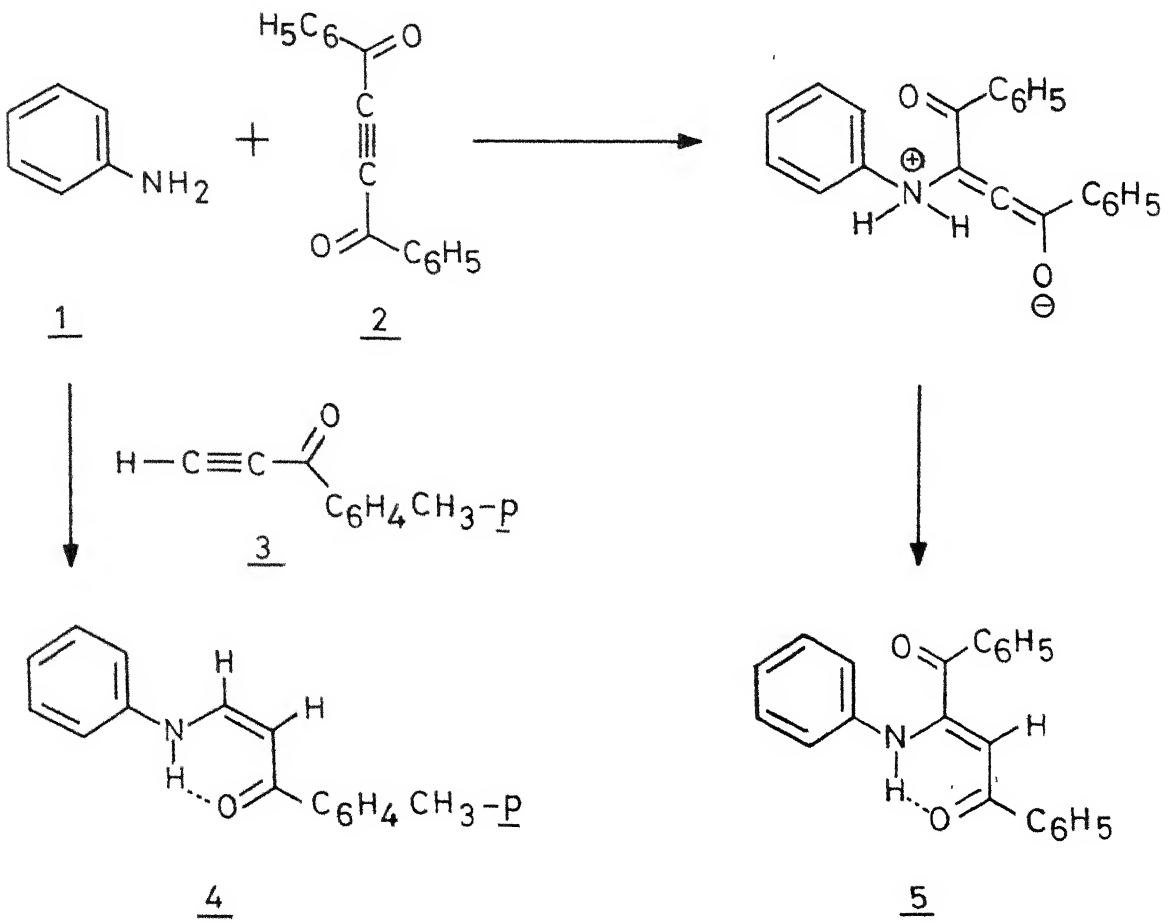
Similarly, aromatic primary amines, such as aniline and its derivatives add to monoaryl and diaryl acetylenic ketones giving rise to 1:1 Michael adducts.[4,9,12-17,20,29-37] The reaction of aniline (1) with dibenzoylacetylene (DBA, 2),

for example, gives 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (5),[35] whereas its reaction with p-toluoylacetylene (3) yields 1-p-tolyl-3-(N-phenylamino)prop-2-en-1-one (4),[36] in excellent yields (Scheme I.1). The stereochemistry across the double bonds in these adducts has been shown to be of the Z-configuration, which has been ascribed to their relative stability due to intramolecular hydrogen-bonding. Mention may be made in this connection that the formation of a 1:2 adduct in the reaction of aniline (1) with DBA has also been reported.[15]

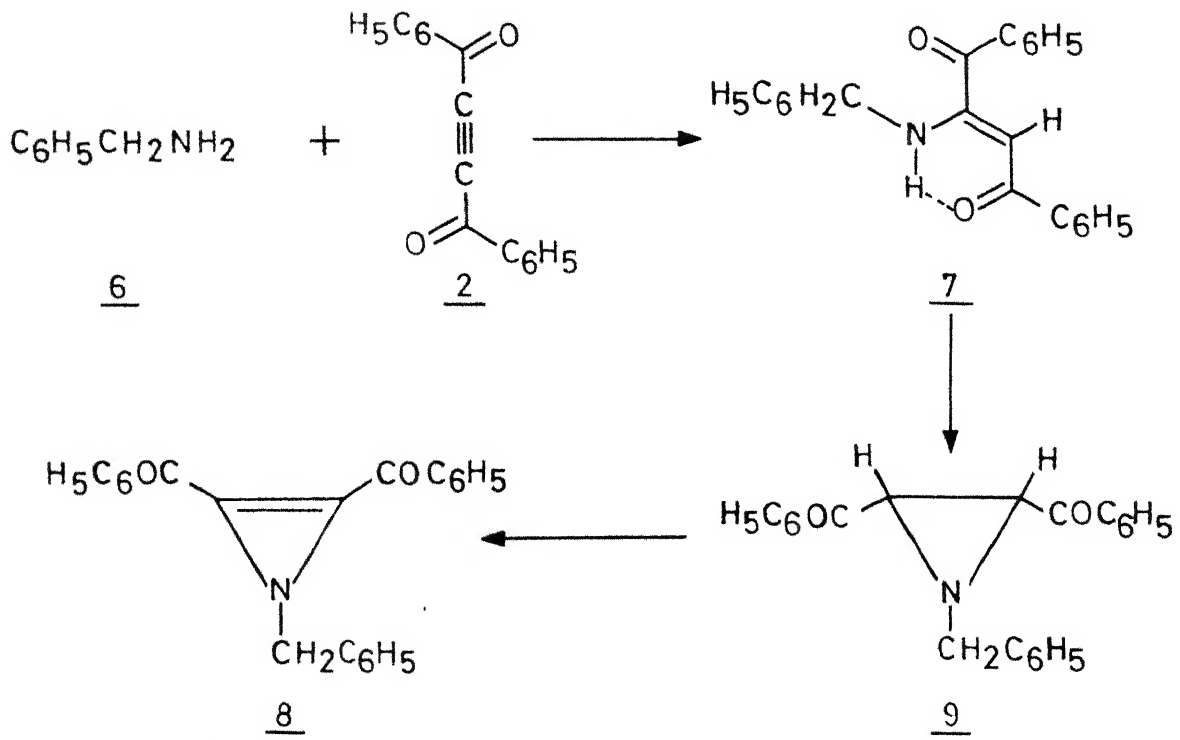
An interesting reaction of benzylamine (6) with DBA has been reported by Titova et al.[16] who have observed that the initially formed 1:1 adduct 7 undergoes an intramolecular nucleophilic addition to give an azirine derivative 8, as shown in Scheme I.2.

The kinetics of addition of primary amines to acetylenic ketones has been studied by several groups of workers[22-26,28,32,33,38,39] and it has been shown that the reaction is invariably of second order and that the reaction rate depends on the basicity of the amine and also on the structural features of the two reactants.[22,23,32,33]

Scheme I.1



Scheme I.2



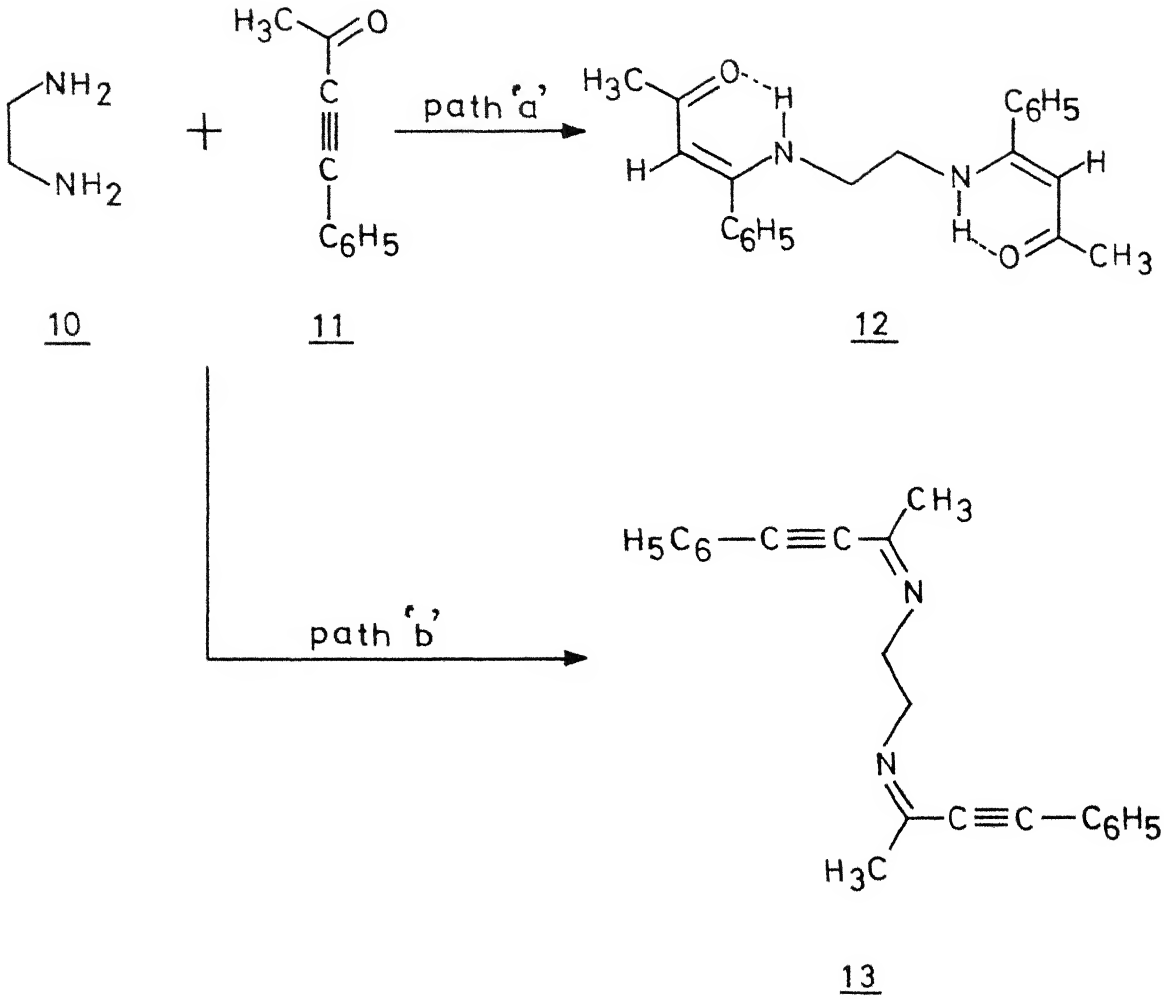
I.2.2 Primary Amines Containing Functional Groups on Adjacent Positions

Aliphatic diamines such as ethylenediamine (10) are reported to react with acetylenic ketones to give different products, depending on the reaction conditions.[14] The reaction of 10 with acetylphenylacetylene (11) in the presence of base, for example, gives a 1:2 adduct, 12, whereas in the absence of a base or in the presence of an acid, the azine 13 is formed (Scheme I.3).[40] In a subsequent investigation, Vereshchagin et al.[41] have shown that ethylenediamine reacts with esters of β-keto acids to give piperazine derivatives.

The reaction of 2-aminoethanethiol (14) with acetylphenylacetylene (11) has been shown to give the 1:1 adduct 15, in which the amino group rather than the more nucleophilic thiol group adds to the acetylenic triple bond (Scheme I.4).[40]

Esters of α-amino acids are known to react with acetylenic monoketones to give simple 1:1 adducts,[42] whereas with acetylenic diketones, besides the 1:1 adducts, the formation of 1:2 adducts has also been reported.[43] In contrast, the reaction with acetylenic γ-hydroxyketones, gives rise to furan derivatives. Thus, the reaction of methyl glycinate (16) with an acetylenic γ-hydroxyketone

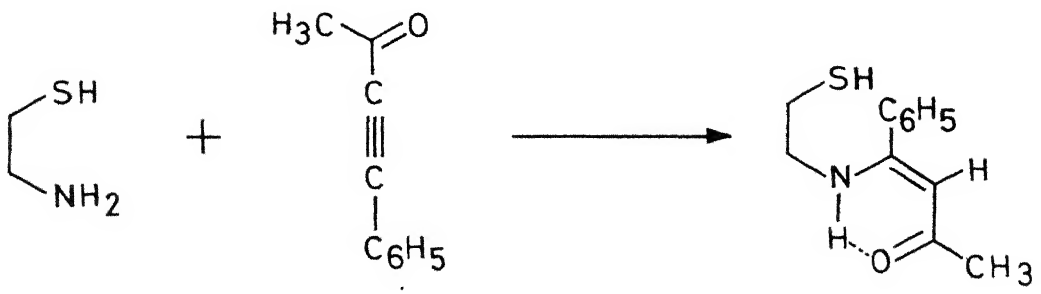
Scheme I.3



10 11 12

13

Scheme I.4

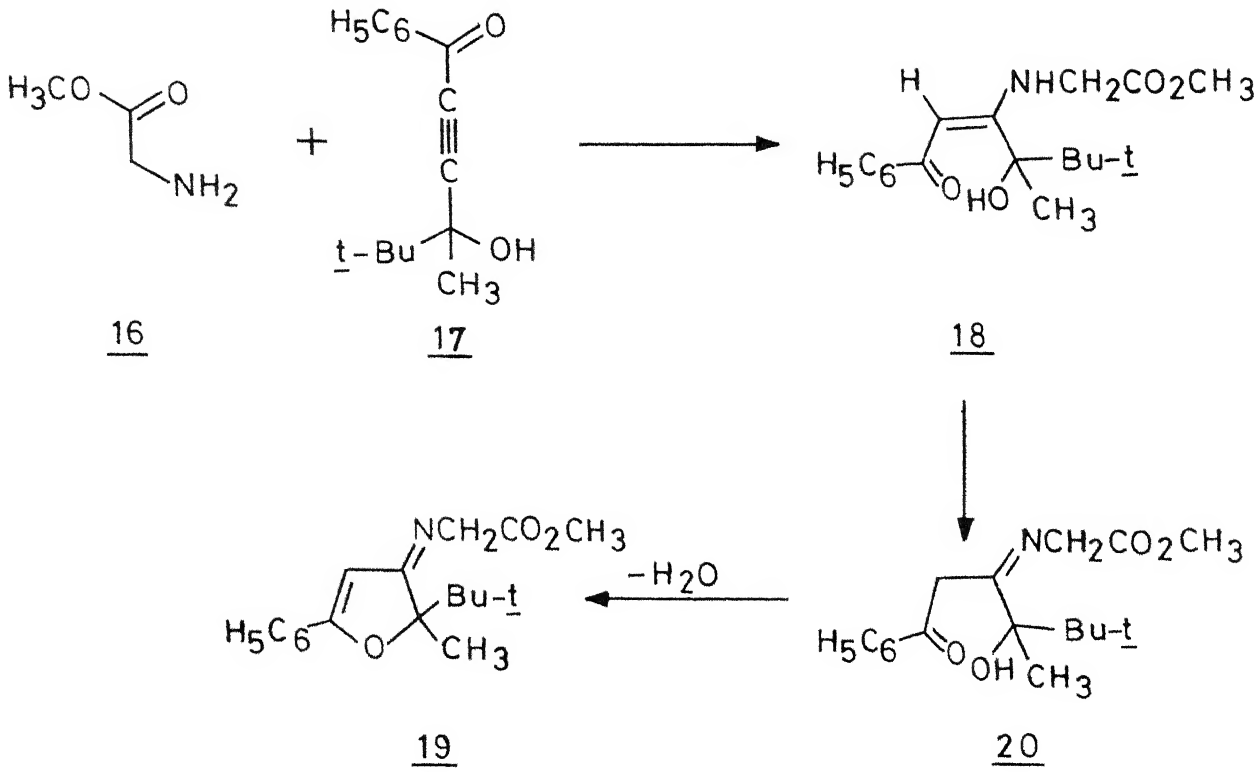


14 11 15

such as 17 gives rise to the furan derivative 19, as shown in Scheme I.5.[42,43] α-Aminoketones, on the other hand, react with acetylenic ketones to give pyrrole derivatives. Thus, the reaction of phenacylamine (21a) with DBA gives rise to the pyrrole derivative 23a (Scheme I.6).[44]

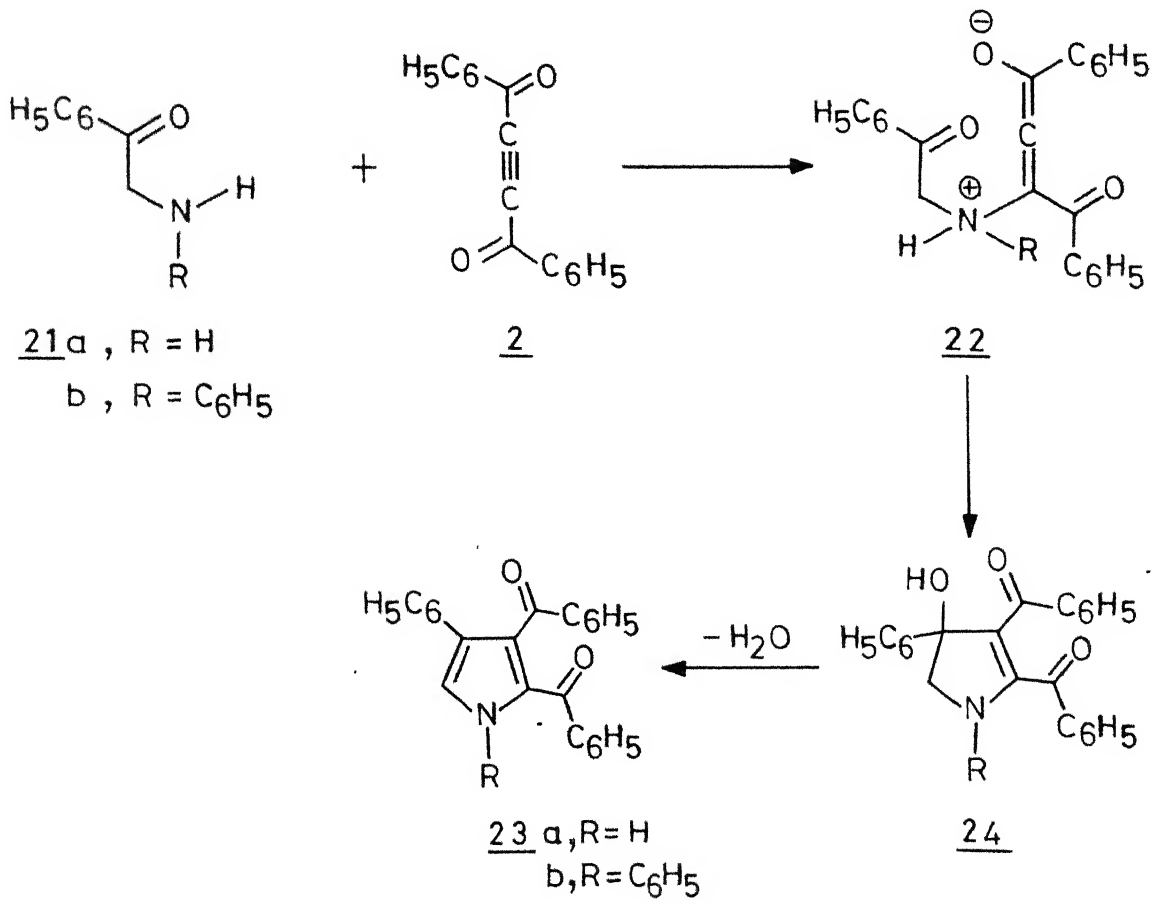
Several groups of workers have studied the reaction of aromatic diamines with acetylenic ketones.[30,35,36,41,45-51] Bindra and LeGoff,[45] for example, have shown that o-phenylenediamine reacts with DBA to give a benzodiazepine derivative. However, subsequent studies[35] have shown that the product formed in this reaction is a quinoxaline derivative and not the benzodiazepine derivative as earlier reported (see, Chapter III for further details). The reaction of 1,8-diaminonaphthalene (25) with DBA, on the other hand, gives rise to a mixture of products consisting of 2-benzoyl-2-phenacyl-2,3-dihydroperimidine (26) and 2-benzoylperimidine (27), as shown in Scheme I.7.[35] However, the reaction of an amino substituted pyridine derivative such as 2-aminopyridine (28) with DBA has been reported to give a mixture of enamine diones namely, 2-(2-imino-1(2H)-pyridyl)-1,4-diphenylbut-2-ene-1,4-dione (31) and 2-(N-2-pyridylamino)-1,4-diphenylbut-2-ene-1,4-dione (29) (Scheme I.8).[35]

Scheme I.5



16 17 18 19 20

Scheme I.6

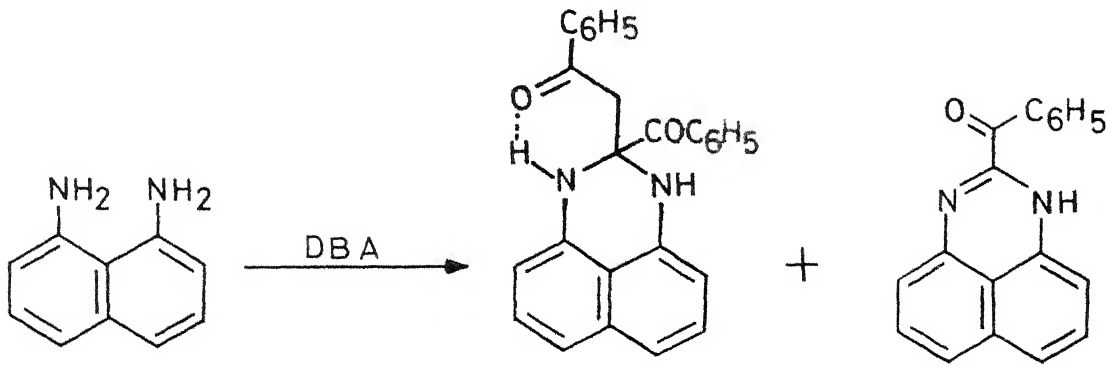


21a , R = H
b , R = C_6H_5

2 22 24

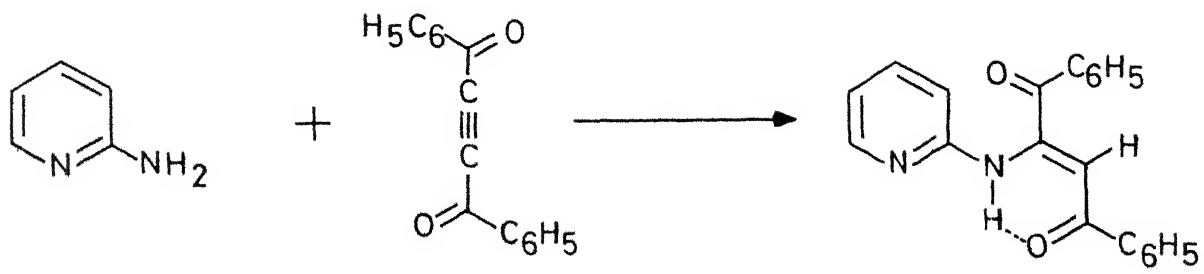
23 a, R = H
b, R = C_6H_5

Scheme I.7

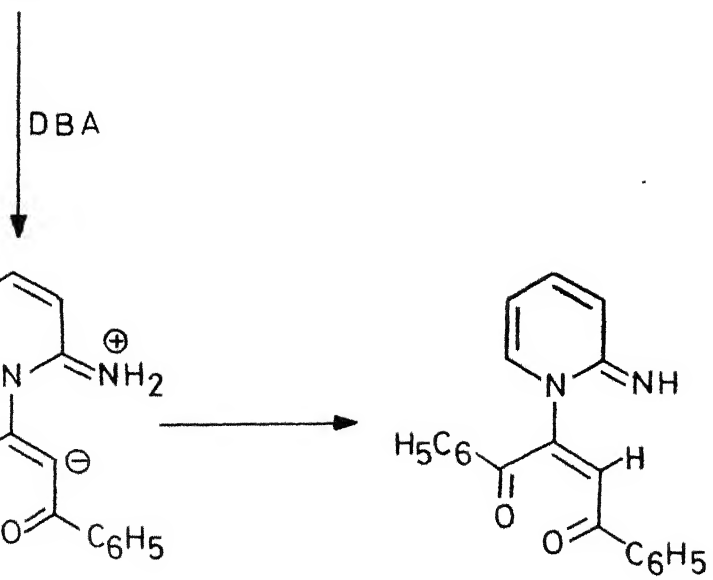


25 26 27

Scheme I.8



28 2 29



30 31

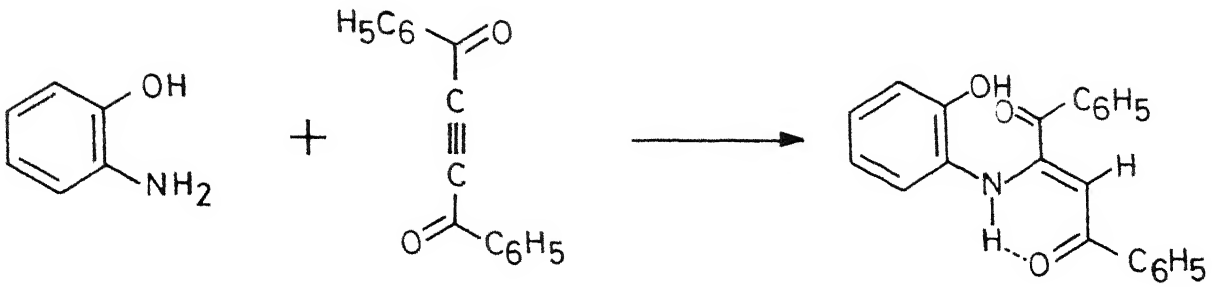
The reaction of o-aminophenol (32) with acetylenic ketones gives the corresponding 1:1 adducts, arising through a nucleophilic addition, involving the amino group.[35,36] The reaction of 32 with DBA, for example, gives rise to 1,4-diphenyl-2-(N-2-hydroxyphenylamino)but-2-ene-1,4-dione (33) (Scheme I.9).[35] However, the reaction of o-aminothiophenol (34) with acetylenic ketones leads to benzothiazepin derivatives. Thus, the reaction of 34 with 4-(diphenylmethoxy)-methyl-1-phenylbut-2-yn-1-one (35) gives 2-(diphenylmethoxy)-methyl-4-phenylbenzothiazepin (36) (Scheme I.10).[46]

In contrast to the reactions of o-aminophenols with acetylenic ketones, the reactions of o-aminoketones with acetylenic ketones provide an excellent synthetic route to heterocyclic compounds. As for example, Potts and Elliott[52] have shown that the reaction of o-aminoacetophenone (37) with DBA gives 2,3-dibenzoyl-4-methylquinoline (39), probably arising through the intermediates 38 and 40, as shown in Scheme I.11.

I.2.3 Secondary Amines

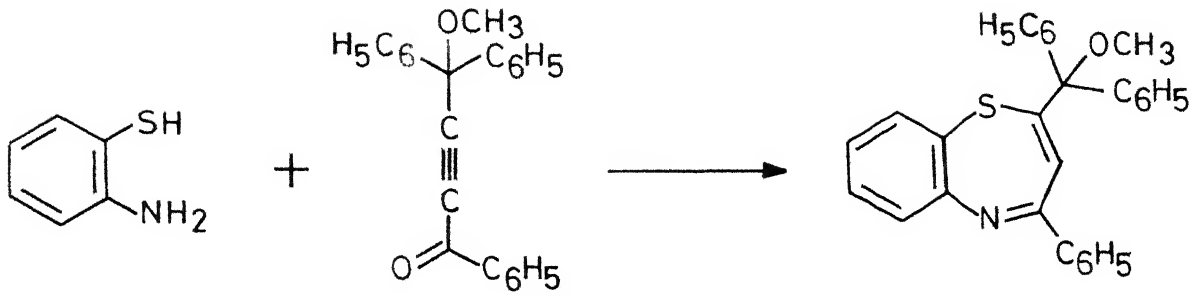
As in the case of primary amines, the nucleophilic addition of secondary amines to acetylenic ketones leads to the formation of 1:1 adducts consisting of α,β-unsaturated β-aminoketones. Secondary amines which have been

Scheme I.9



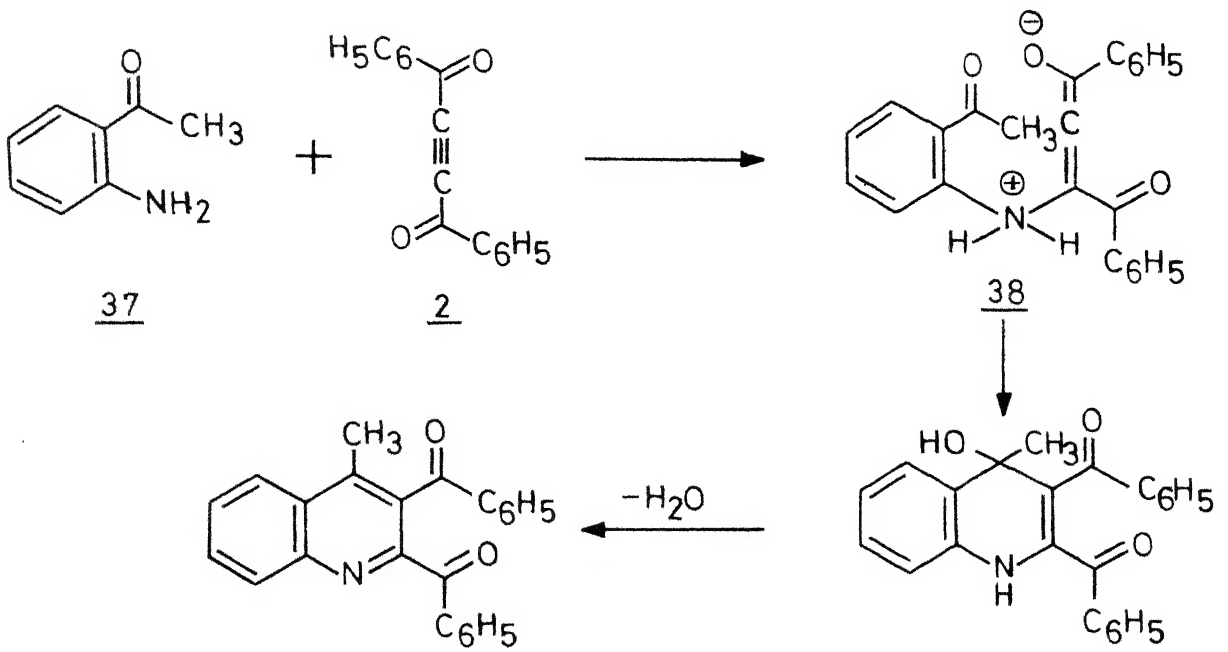
32 2 33

Scheme I.10



34 35 36

Scheme I.11



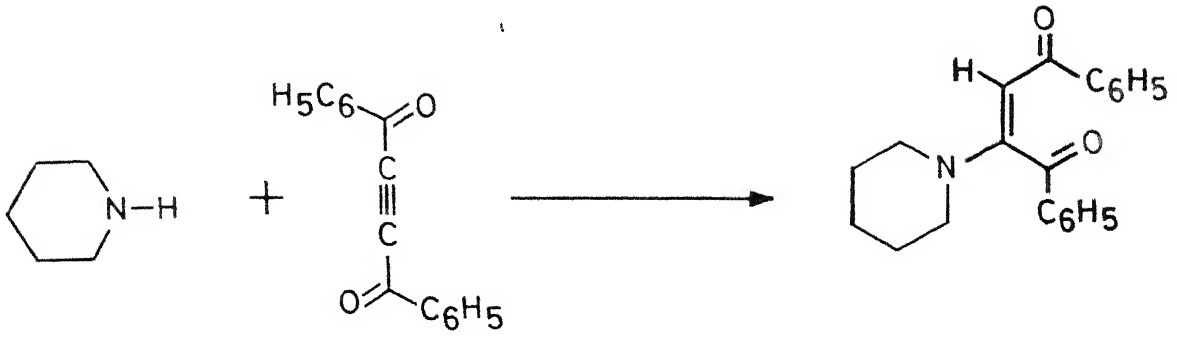
37 2 38 40 39

extensively studied include dimethylamine,[4,13,15] diethylamine,[2-4,10,14,15,20,28,32,53,54] piperidine,[2,4,12,14,17,25,29,30,34-36,55] aziridine[55,56] and several other amine derivatives.[2,11,14-17,23-26,28,34-36,55,57-66] The reaction of piperidine (41) with DBA, for example, has been recently reported to give 1,4-diphenyl-2-(N-piperidino)but-2-ene-1,4-dione (42) and this adduct has been found to be of the E-configuration, on the basis of UV spectral correlations (Scheme I.12).[35] In general, it has been observed that the addition of secondary amines to DBA proceed in a stereospecific manner and arising through a cis-mode of addition.[11,35,36]

Heine et al.[60] have shown that the reaction of diaziridines with DBA gives rise to products in which the diaziridine ring is no longer intact. Thus, in the reaction of 3,3-pentamethylenediaziridine (43) with DBA, the initially formed adduct 44 undergoes facile conversion to the enamine adduct 46, which isomerises to the imine tautomer 45 (Scheme I.13).

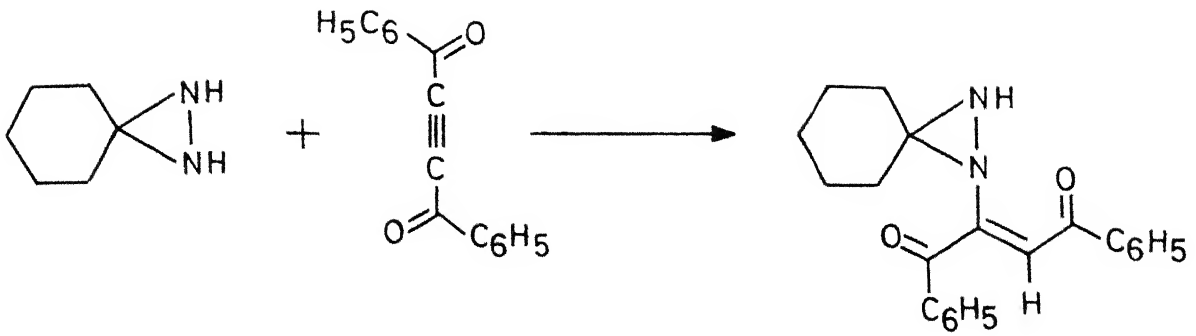
Secondary amines with appropriate functional groups on adjacent positions can give rise to heterocyclic compounds. Thus, it has been shown that phenacylaniline (21b) reacts with DBA to give 2,3-dibenzoyl-1,4-diphenylpyrrole (23b), as shown in Scheme I.6.[35]

Scheme I.12

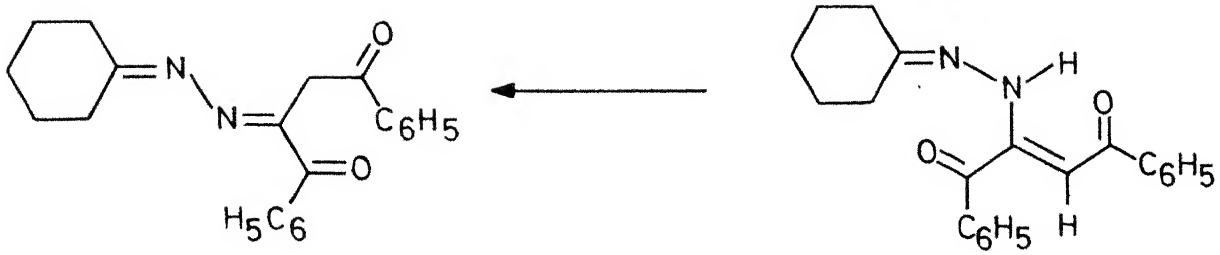


41 2 42

Scheme I.13



43 2 44



45 46

I.2.4 Tertiary Amines

Salts of tertiary amines are known to react with acetylenic ketones to give quaternary ammonium salts of the corresponding 1:1 adducts in good yields.[67,68] Thus, it has been observed that benzoylacetylene, for example, reacts with trimethylammonium chloride in presence of trimethylamine to give benzoylvinyltrimethylammonium chloride.[67]

I.2.5 Hydrazines, Hydrazides and Hydrazones

a Hydrazines

Numerous examples are known in which the reaction of hydrazine with acetylenic ketones has been utilized for the synthesis of pyrazoles.[31,60,69-77,82] Heine et al.[60], for example, have reported the formation of 5-benzoyl-3-phenylpyrazole in the reaction of hydrazine with DBA. Similarly, phenylhydrazine has been shown to react with acetylenic ketones to form 1:1 adducts,[29] which subsequently undergo ring closure, to give the corresponding pyrazoles.[12,69,72-74,78] Engelmann and Kirmse[78] had shown, on the basis of NMR studies, that the adduct 49b formed from phenylhydrazine and benzoylacetylene (48) has the E-configuration, which in the presence of acids is isomerised to the Z-isomer, 51b. Subsequent cyclization of 51b leads to 3,5-diphenylpyrazole (50b), as

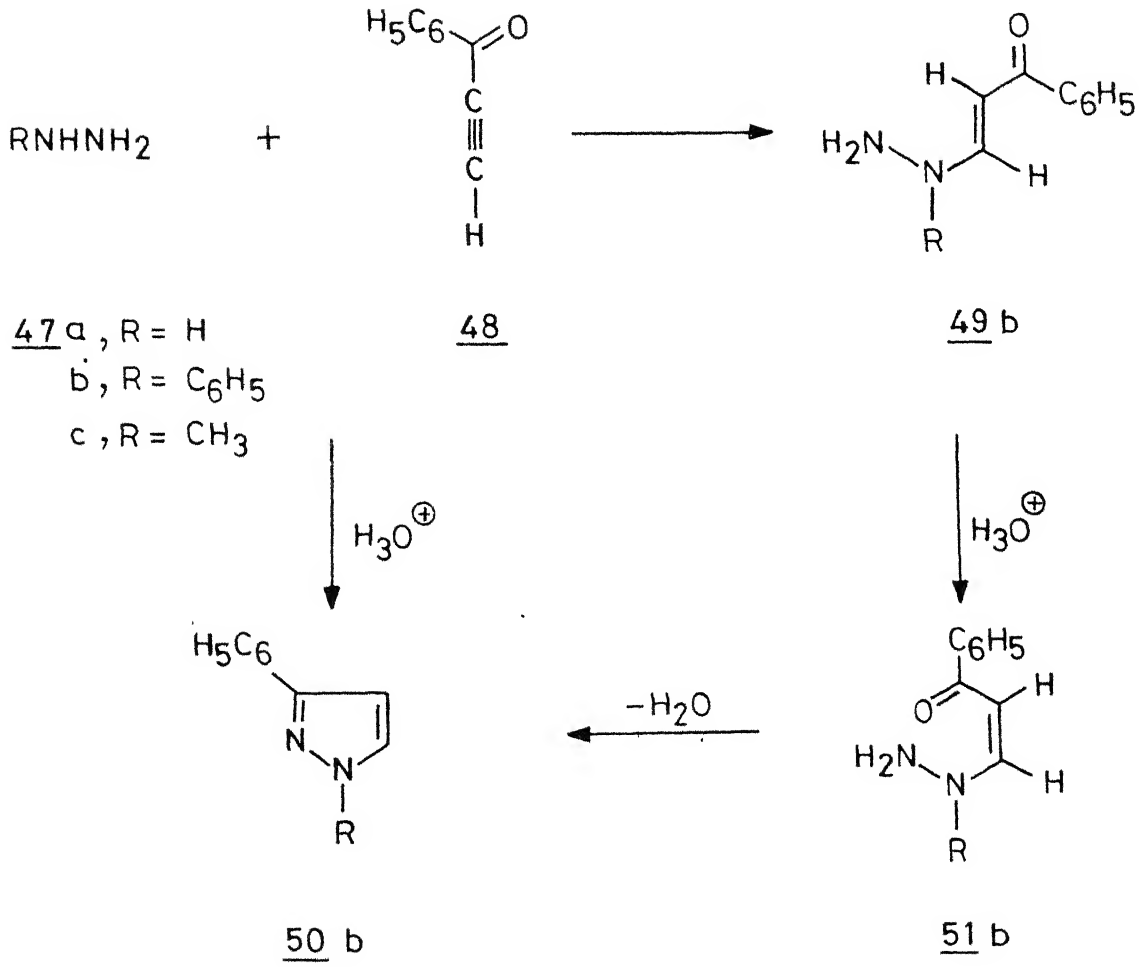
shown in Scheme I.14. Similarly, the reactions of methylhydrazine[60,74,79,80] and n-butylhydrazine[60] with acetylenic ketones have been shown to give the corresponding pyrazole derivatives. In contrast, the reaction of N,N-dimethylhydrazine with acetylenic ketones gives rise to the corresponding 1:1 adducts.[74,80,81]

b Hydrazides

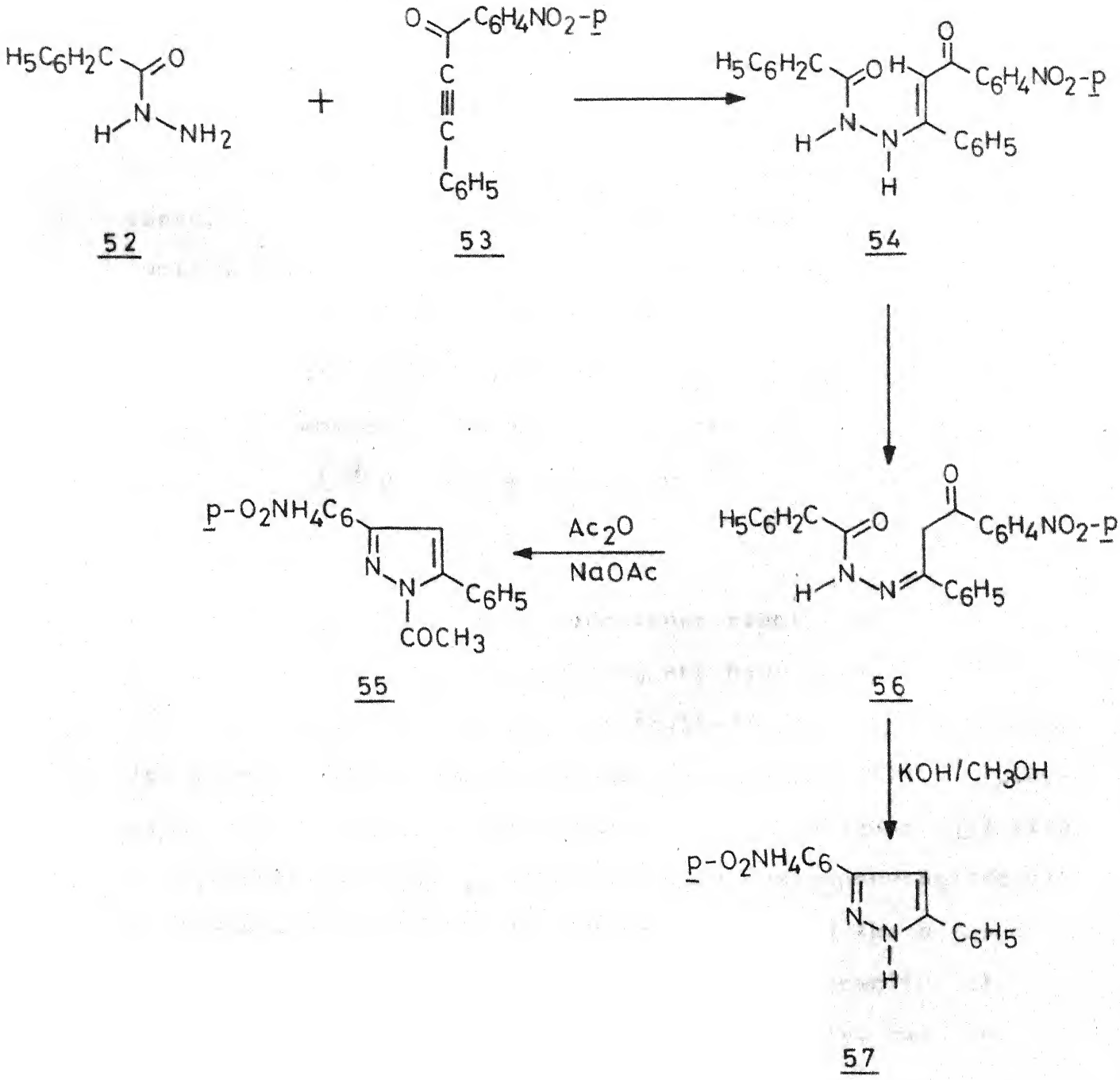
El-Rayyes and Al-Hajjar[74] and others[79,80] have shown that aliphatic and aromatic acid hydrazides react with acetylenic ketones to give the corresponding N-acyl or N-aroylhydrazones, which undergo different modes of cyclization, depending on the reaction conditions. Thus, phenylacetic acid hydrazide (52) reacts with p-nitrobenzoylphenylacetylene (53) to give 3-(2'-phenacylhydrazono)-1-(p-nitrophenyl)-3-phenylpropan-1,3-dione (56), which in the presence of acetic anhydride cyclizes to give 1-acetyl-3-(p-nitrophenyl)-5-phenylpyrazole (55). However, when 56 is treated with methanolic potassium hydroxide, it leads to 3-(p-nitrophenyl)-5-phenylpyrazole (57) (Scheme I.15).

Engelmann and Kirmse[78] have shown that p-toluenesulfonic acid hydrazide (58) reacts with benzoylacetylene (48) to give different products, depending on the reaction conditions. The reaction of 58 with 48 in the presence of

Scheme I.14


RNHNH2
+
H5C6
O
C
C
H
H
O
C6H5
H2N
N
H
R
47 a , R = H
b , R = C6H5
c , R = CH3
48
49 b
H3O⊕
H3O⊕
H5C6
N
N
R
-H2O
C6H5
O
H
H2N
N
H
R
50 b
51 b

Scheme I.15


H5C6H2C
O
N
H
NH2
52
+
O
C6H4NO2-P
C
C
C6H5
53
H5C6H2C
O
H
O
C6H4NO2-P
N
H
N
H
C6H5
54
H5C6H2C
O
O
C6H4NO2-P
N
H
N
C6H5
56
Ac2O
NaOAc
P-O2NH4C6
N
N
C6H5
COCH3
55
KOH/CH3OH
P-O2NH4C6
N
N
H
C6H5
57

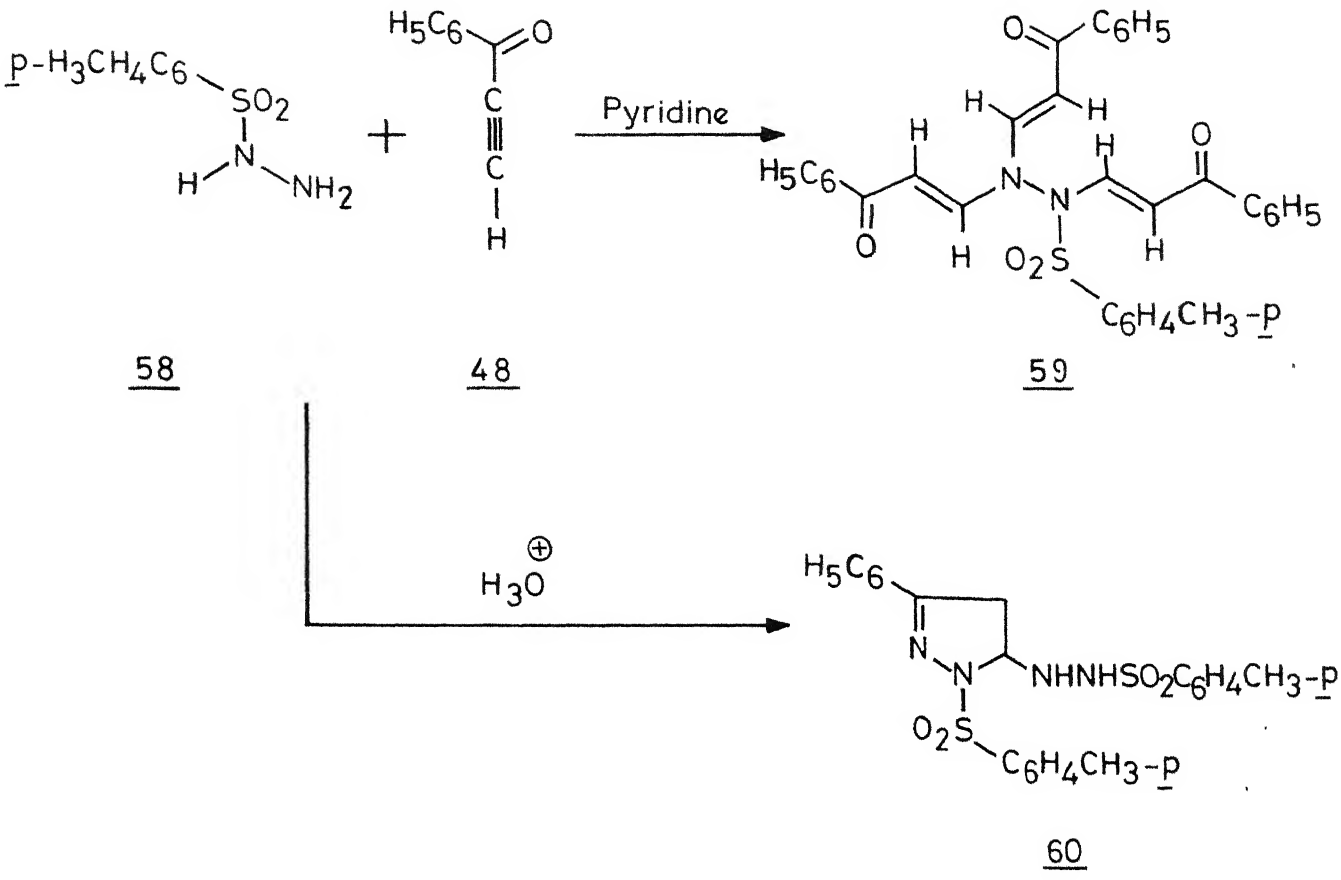
pyridine, for example, gives a 1:3 adduct, 59, whereas in the presence of acidic catalysts, a 2:1 adduct, 60, is formed (Scheme I.16).

Acetylenic ketones react with aliphatic and aromatic hydrazinecarboxylates such as ethyl hydrazinecarboxylate and phenyl hydrazinecarboxylate to give the corresponding hydrazones,[80,83] which, under different reaction conditions, cyclize to give pyrazoles. For example, the treatment of these hydrazones with acetic anhydride gives the corresponding 1-ethoxycarbonyl and 1-phenoxycarbonyl substituted pyrazoles, while in the presence of an acid or basic catalyst, 1-unsubstituted pyrazoles are formed.[83]

c Hydrazones

Aldehyde and ketone hydrazones react with acetylenic ketones to give the corresponding ene-hydrazones.[60,84,85] The reaction of benzaldehyde methylhydrazone (61) with DBA, for example, gives the 1:1 adduct 62 (Scheme I.17).[84] Likewise, the reaction of benzaldehyde benzylhydrazone (63) with acetylacetylene (64) gives rise to the corresponding adduct 65 (Scheme I.18).[84,85] It has been shown, on the basis of NMR studies, that the adducts formed in the reaction of hydrazones with aryl ethynylketones, generally, have the E-configuration.

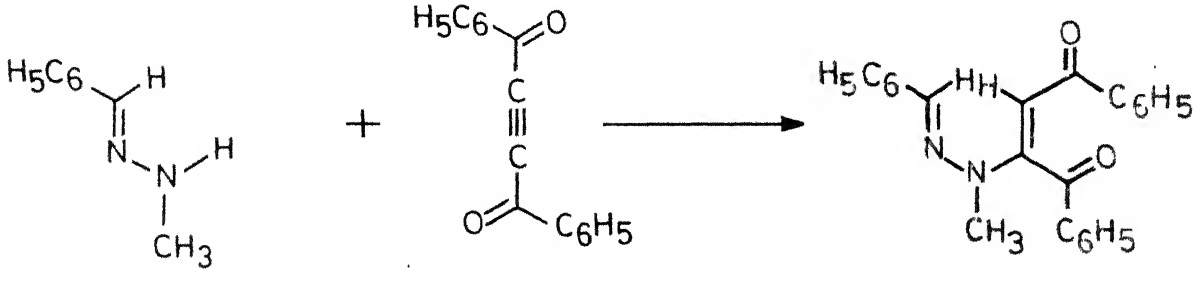
Scheme 1.16



58 48 59

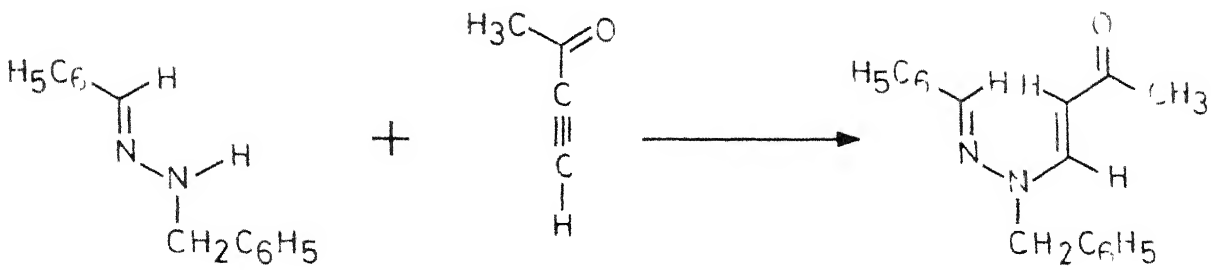
60

Scheme 1.17



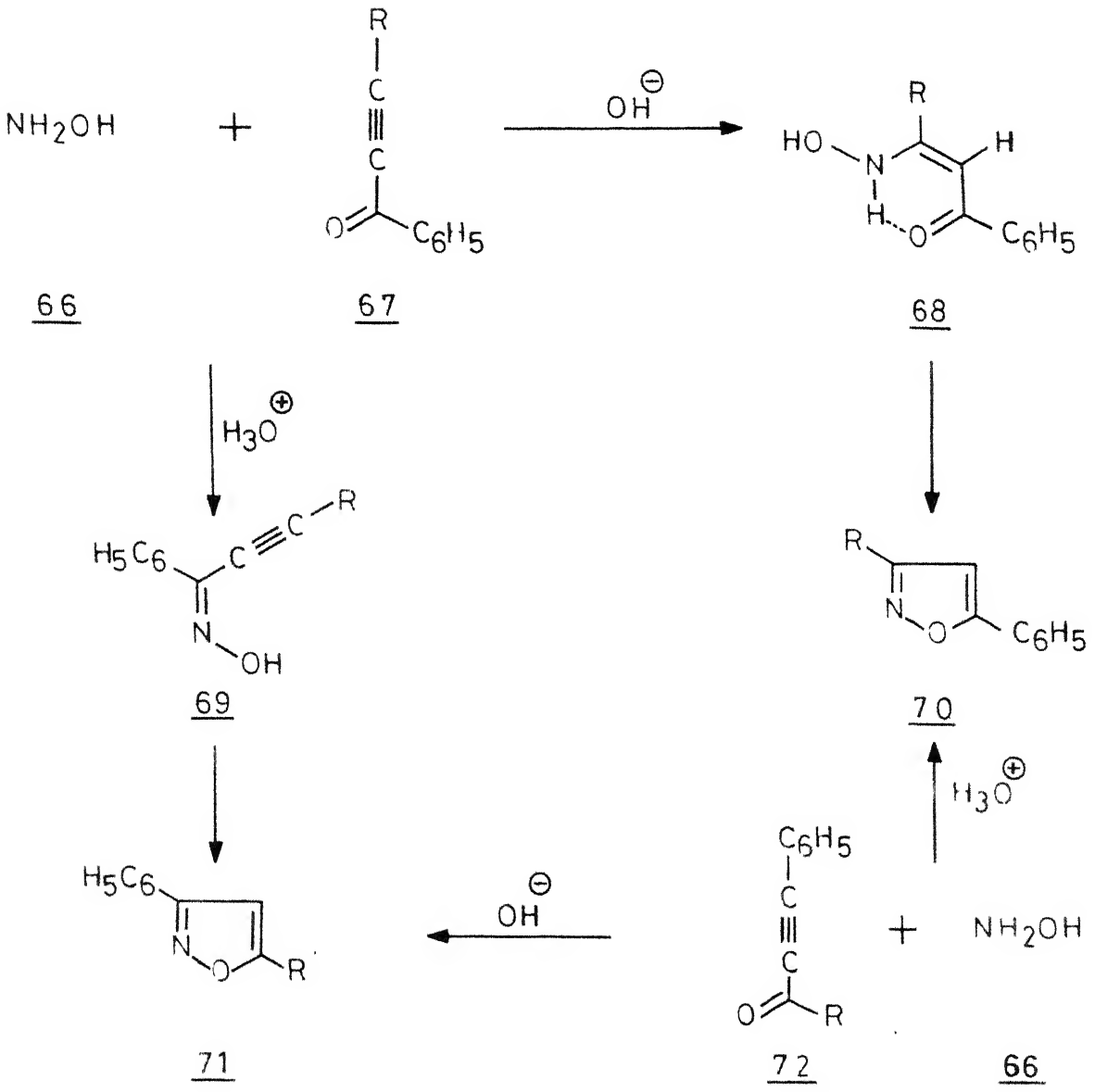
61 2 62

Scheme I.18



63 64 65

Scheme I.19



66 67 68 69 70 71 72 66

R = $H_4C_6CH_3$-p

I.2.6 Hydroxylamine

The reaction of hydroxylamine (66) with acetylenic ketones has been studied extensively for the synthesis of isoxazoles.[29,31,70-72,75,77,86-89] The reaction of 66 with DBA, for example, gives a nearly quantitative yield of 3,5-diphenylisoxazole.[77] It has been observed that the mode of addition of 66 to acetylenic ketones is dependent on the reaction conditions. Thus, the reaction of 66 with 67 in alcoholic alkaline medium leads to the formation of 3-(p-anisyl)-5-phenylisoxazole (70), whereas in acidic medium, 5-(p-anisyl)-3-phenylisoxazole (71) is formed. It has been assumed that in alkaline medium, the reaction proceeds through 68, whereas in presence of acids, 69 is formed, which cyclizes to give 71, as shown in Scheme I.19. This assumption, however, has been supported by the observation that the reaction sequence is exactly reversed when p-anisoylphenylacetylene (72) is used instead of 67, under the same reaction conditions.[88]

I.2.7 Amides, Ureas, Thioureas, Guanidines, Semicarbazides, Enamines and Related Systems

a Amides

Formamide has been reported to react with acetylenic ketones in a 2:1 ratio, giving rise to pyrimidine derivatives.

The reaction of formamide (73) with benzoylphenylacetylene (74), for example, gives rise to 4,6-diphenylpyrimidine (75) (Scheme I.20).[90] Similarly, cyanoacetamide has been found to react with 74 to give 3-cyano-4,6-diphenyl-2(1H)-pyridone.[91,92]

b Ureas

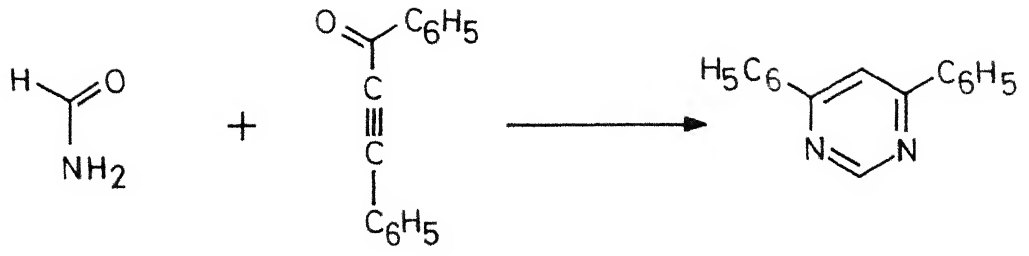
Similar to the reactions of amides, ureas are known to react with acetylenic ketones to give the corresponding pyrimidinones.[83,93,94] Urea (76a), for example, reacts with benzoylphenylacetylene (74) in the presence of a strong base such as sodium ethoxide, to give 4,6-diphenyl-2(1H)-pyrimidinone (78a), as shown in Scheme I.21.[83]

c Thioureas

Thiourea and substituted thioureas are reported to undergo nucleophilic additions to acetylenic ketones to yield pyrimidinethiones.[80,83,93,95] Benzoylphenylacetylene (74), for example, reacts with thiourea (76b) in the presence of sodium ethoxide to give 4,6-diphenylpyrimidine-2(1H)-thione (78b), by the elimination of elements of water from the initially formed 1:1 adduct, 77b, as shown in Scheme I.21.[83]

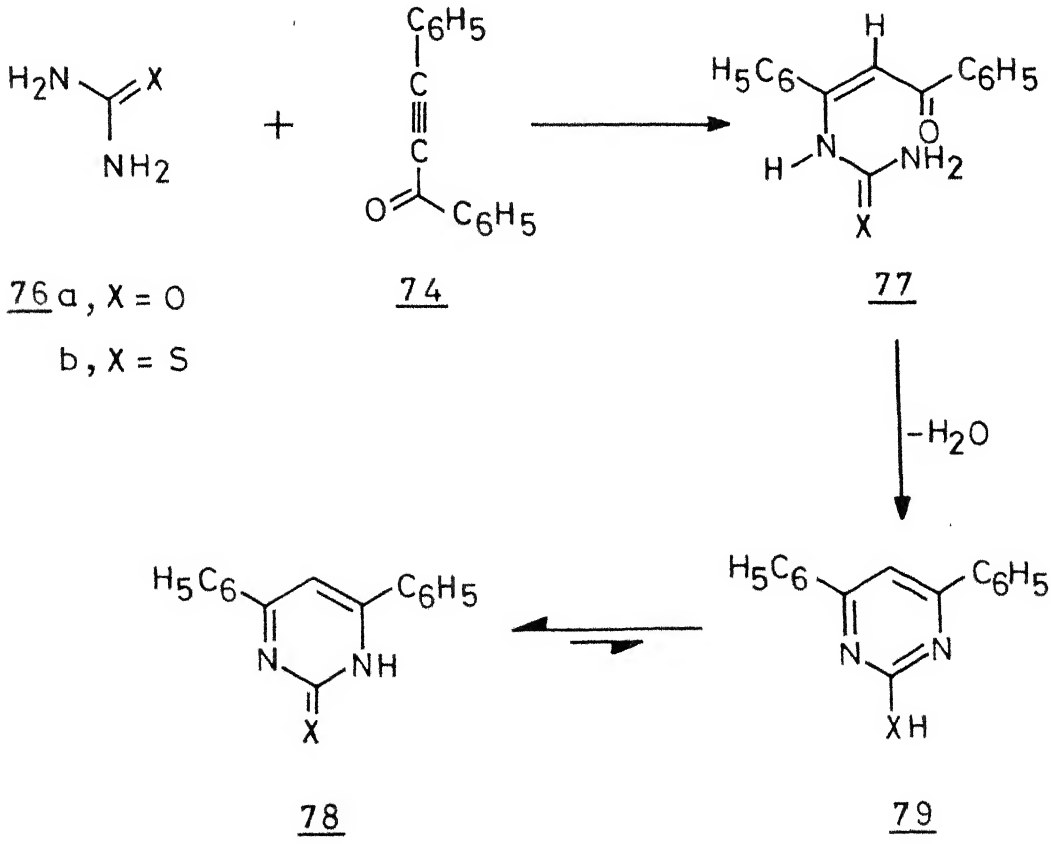
Nakhmanovich et al.[76] have shown that thiourea (76b) reacts with acetylenic ketones (80) to form 1:1 adducts (81), by the nucleophilic attack through sulfur instead of nitrogen (Scheme I.22). In the presence of excess of acetylenic ketones,

Scheme I.20



73 74 75

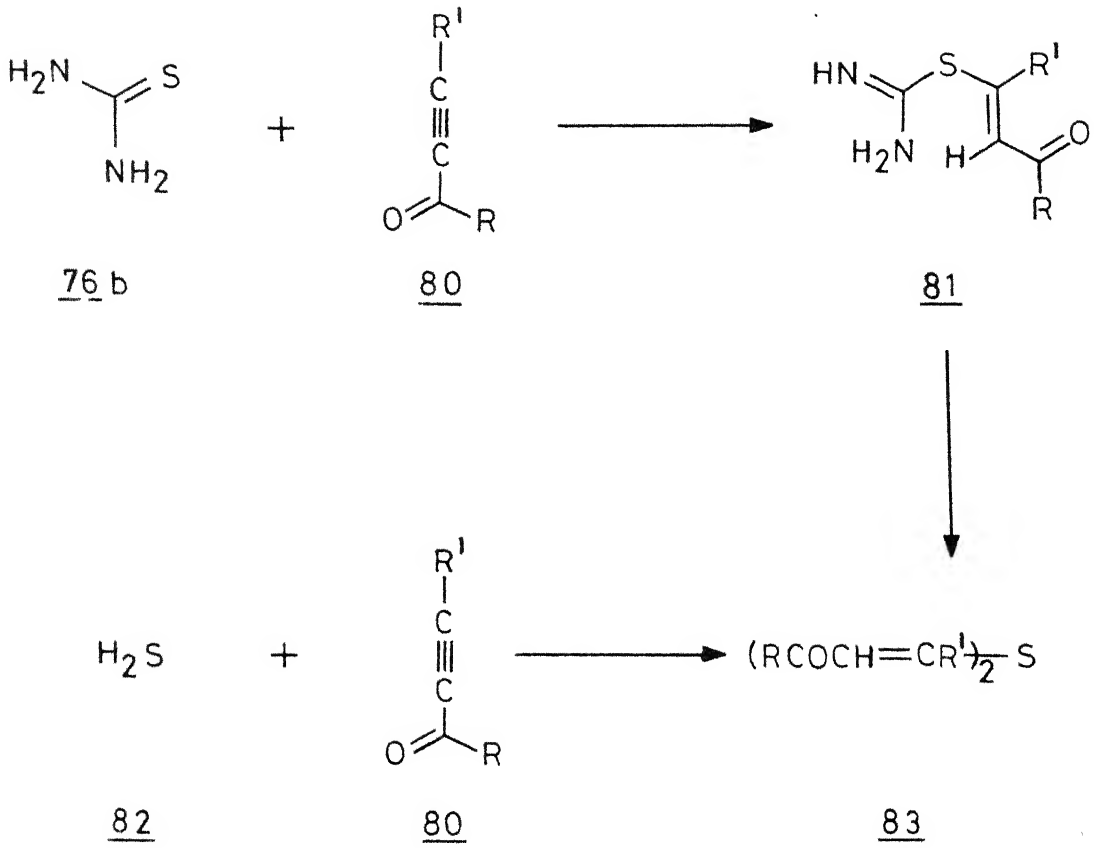
Scheme I.21



76 a, X = O
b, X = S

74 77 78 79

Scheme I.22



R = CH_3 , 2-thienyl , C_6H_5

R^1 = H , $(CH_2)_3\ CH_3$, C_6H_5 , 2-thienyl

however, sulfides (83) are formed, which in turn are also formed through the nucleophilic addition of hydrogen sulfide to the corresponding acetylenic ketones (80).

Baddar et al.[95] have shown that allylthiourea reacts with aroylphenylacetylenes to give 1-allyl-4,6-diarylpyrimidine-2(1H)-thione. S-Benzylisothiourea (84), on the other hand, reacts with benzoylphenylacetylene (74) to give α-benzoyl-β-benzylmercaptostyrene (86) (Scheme I.23).[95]

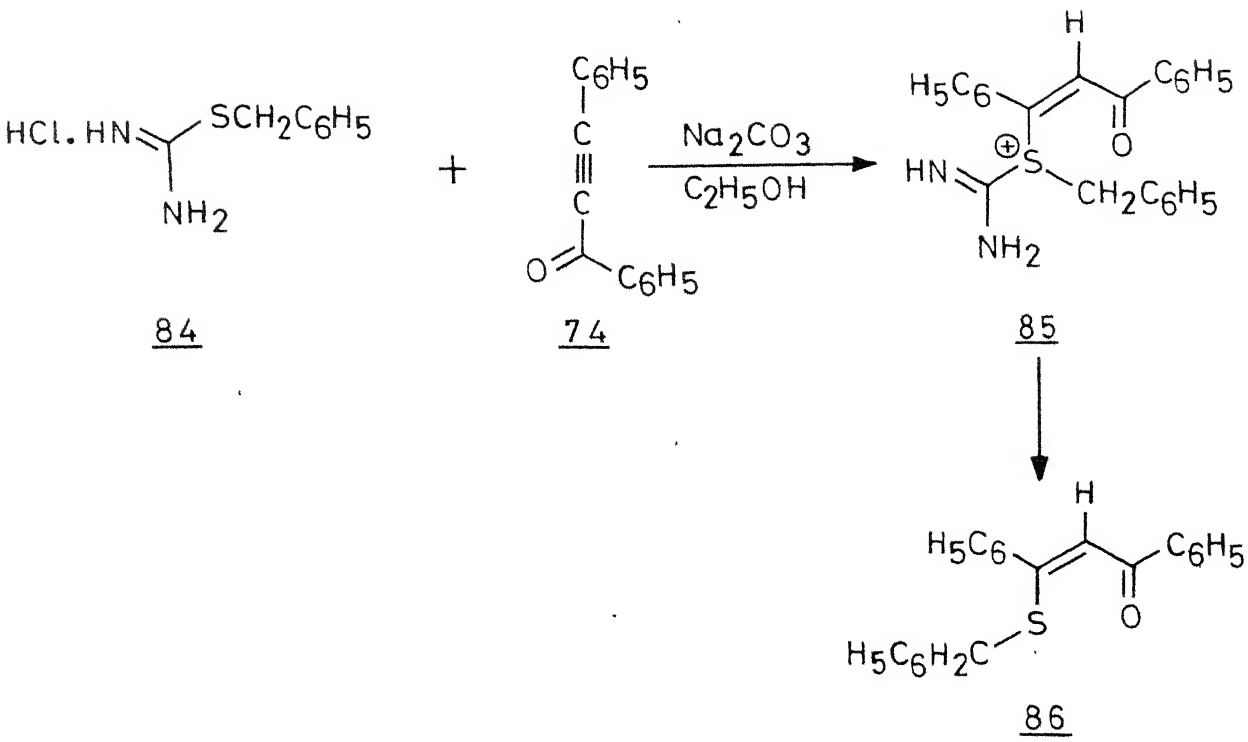
d Guanidines

The reaction of guanidine (87) with acetylenic ketones has been found to yield 2-aminopyrimidines.[31,74,80,83] Guanidine (87) when treated with benzoylphenylacetylene (74), for example, gives rise to 2-amino-4,6-diphenylpyrimidine (88) (Scheme I.24).[83]

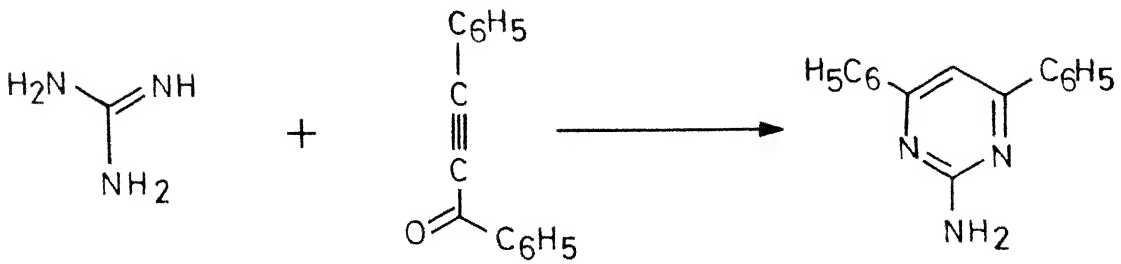
e Semicarbazides

Semicarbazides behave like hydrazines in their reaction with acetylenic ketones. Phenylsemicarbazide (89), for example, reacts with 5-(2-pyranyloxy)hex-3-yn-2-one (90) to give 3-(1-hydroxyethyl)-5-methylpyrazole (91), as shown in Scheme I.25.[96]

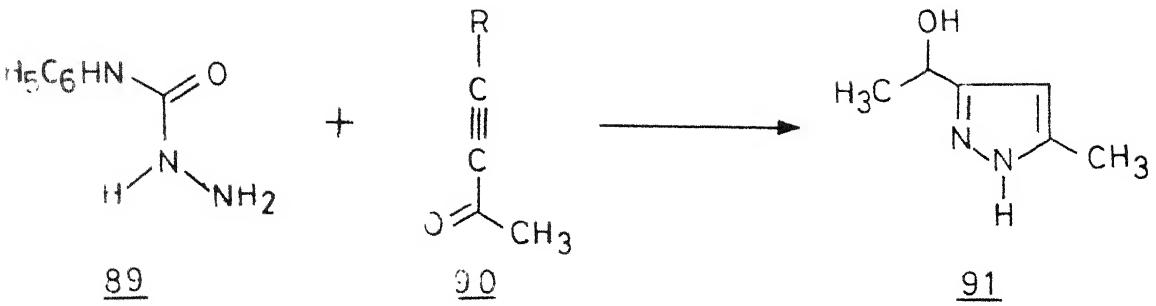
Scheme I.23



Scheme I.24

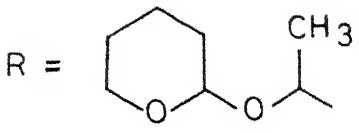


Scheme I 25

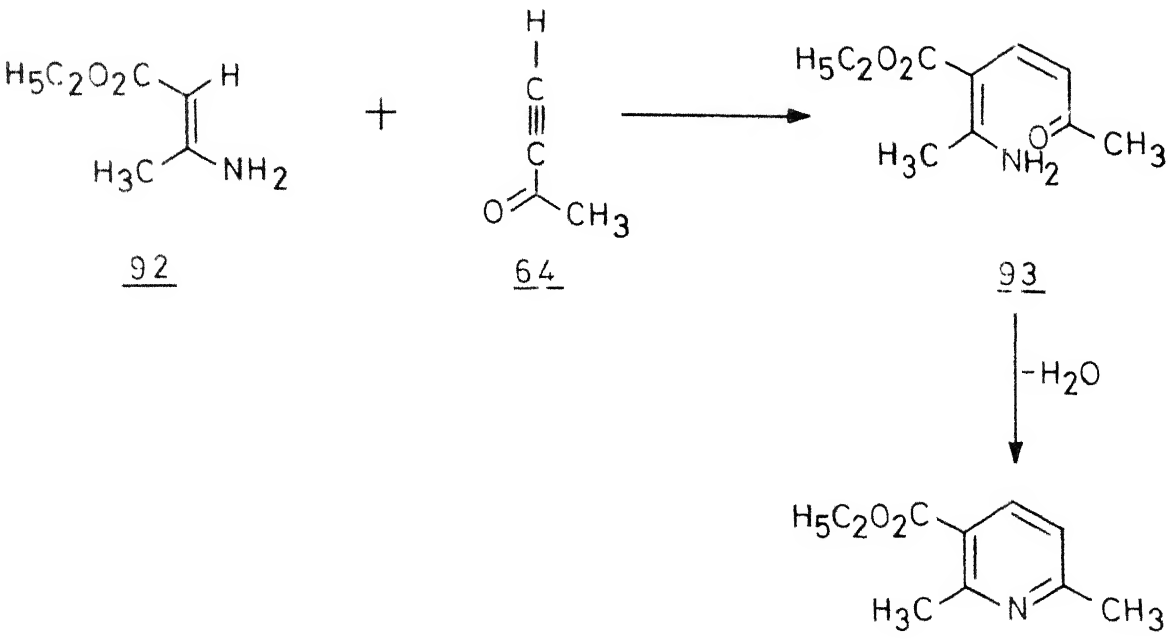


89 90 91

R =



Scheme I.26



92 64 93 94

f Enamines and Related Systems

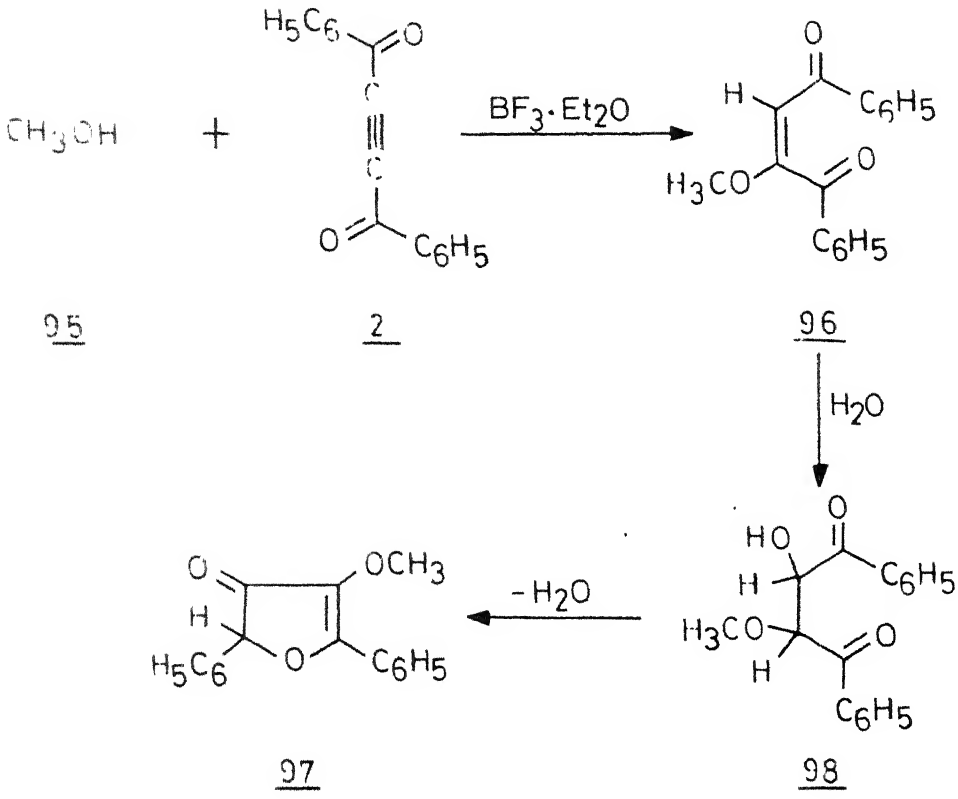
Bohlmann and Rahtz[97] have shown that ethyl β-aminocrotonate (92) reacts with acetylenic ketones to give nicotinic acid derivatives. Thus, the reaction of 92 with but-1-yn-3-one (64) gives rise to ethyl 2,6-dimethylpyridine-3-carboxylate (94), as shown in Scheme I.26. The formation of 94 in the reaction of 92 and 64 has been rationalized in terms of the initial formation of the 1:1 adduct 93, which subsequently loses elements of water.

I.3 OXYGEN CONTAINING NUCLEOPHILES

I.3.1 Hydroxy Compounds

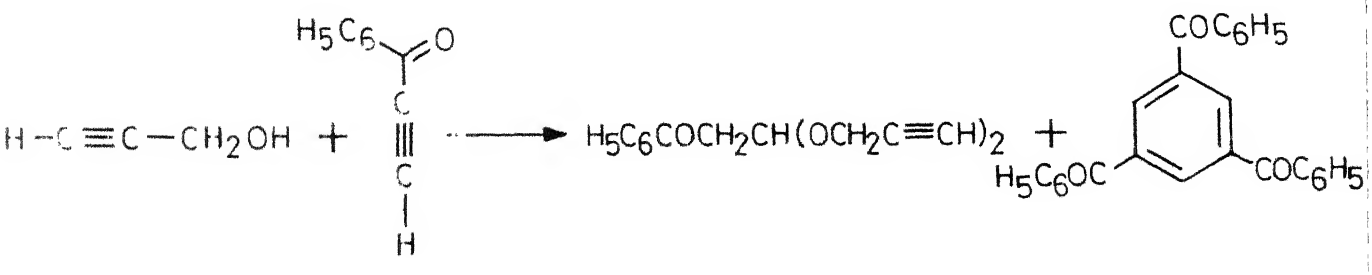
Unlike the reactions of amines, the addition of alcohols to acetylenic ketones takes place only in the presence of basic catalysts such as alkoxides[3,16,37,98-103] and tertiary amines[37,101,103] to give alkoxyvinyl ketones, whereas furan derivatives are formed in the presence of boron trifluoride.[16,37,102] The reaction of methyl alcohol with DBA in the presence of boron trifluoride etherate, for example, leads to the formation of 3-methoxy-2,5-diphenyl-4,5-dihydro-4-furanone (97), presumably through the intermediates 96 and 98, as shown in Scheme I.27.[37] Similarly, tert-butanol has been reported to react with DBA in the presence of boron trifluoride to form 2,5-diphenyl-3,4(2H,5H)-furandione.

Scheme I.27



95 2 96 98 97

Scheme I.28



99 48 100 101

Vereshchagin et al.[104] have recently shown that acetylenic alcohols such as propargyl alcohol and 3-phenyl-prop-1-yn-3-ol react with acetylenic ketones in the presence of sodium to give simple 1:1 adducts. However, the reaction between benzoylacetylene (48) and excess of propargyl alcohol (99), in the presence of sodium gives a mixture of products consisting of the 1:2 adduct 100 and 1,3,5-tribenzoylbenzene (101) (Scheme I.28).[104] The formation of 101 in this reaction can be explained in terms of a base-catalyzed trimerization of 48. Walia and Walia[105] have also reported the formation of 2:1 adducts in the reaction of methanol with acetylacetylene in the presence of either cyanide or carbonate ion as catalyst. Eaton and Stubbs[106] have shown that the addition of alcohols to ethynyl ketones generally proceed through a cis-stereochemistry. In the reaction of alcohols to silyl ethynyl ketones, the nucleophilic addition leads to products, arising through a cleavage of the carbon-silicon bond.[107]

Phenols, likewise, react with acetylenic ketones to give 1:1 adducts[3,16,37,102,103,108] or furan derivatives,[16,37,102] depending on the reaction conditions. Venkataramani et al.[108] have recently shown that the addition of phenol to benzoylacetylene, for example, gives rise to 3-phenoxy-1-phenylprop-2-en-1-one, having a trans-stereochemistry across the double bond.

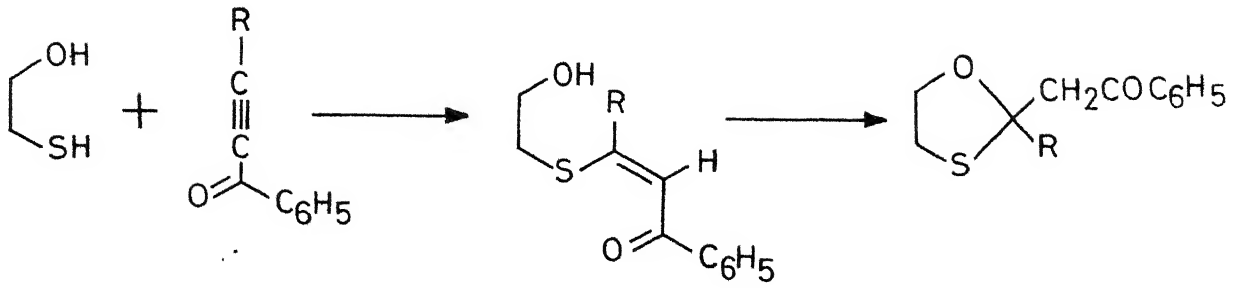
I.3.2 Hydroxy Compounds Containing Functional Groups on Adjacent Positions

Elokhina et al.[109,110] have studied the reaction of β-mercaptoethanol (102) with acetylenic ketones and have shown that, in general, 1:1 adducts are formed in these reactions. Thus, the reaction of 102 with n-butylbenzoylacetylene (103b) gives the 1:1 adduct 104b (Scheme I.29).[110] Similarly, the reaction of 102 with benzoylphenylacetylene (103a) gives the 1:1 adduct, 104a, which in turn has been shown to undergo an intramolecular cyclization to give 2-phenacyl-2-phenyl-1,3-oxathiolane (105a), either on heating alone or in the presence of basic catalysts such as potassium carbonate (Scheme I.29).[111]

Similarly, ethylene glycol (106) adds to different acetylenic ketones to give 1:1 adducts, which cyclize to give the corresponding 1,3-dioxolanes. The reaction of 106 with benzoylphenylacetylene (74), for example, leads to 2-phenacyl-2-phenyl-1,3-dioxolane (108) (Scheme I.30).[103]

An α-ketoalcohol such as hydroxyacetone (109) reacts with benzoylacetylene (48) in the presence of potassium carbonate to give a mixture of products consisting of the furan derivative 112 and 1,3,5-tribenzoylbenzene (101).[104] It is presumed that the initially formed 1:1 adduct, 110, undergoes cyclization to the hydroxyfuran

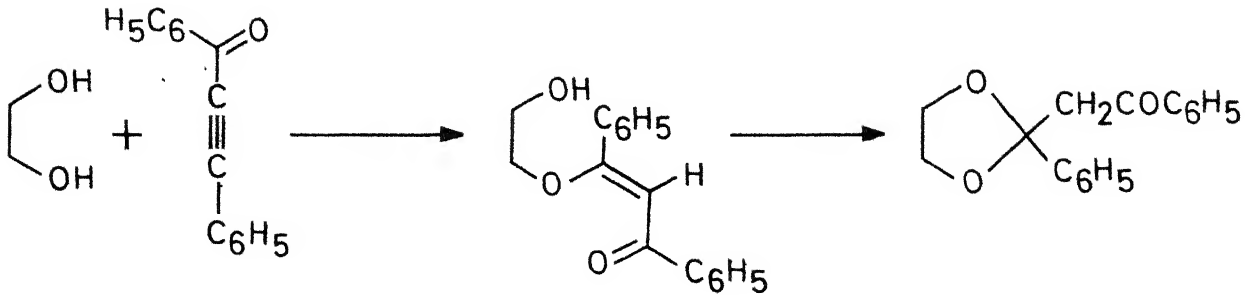
Scheme I.29



102 103 a, R = C_6H_5 104 a,b 105a

b, R = $(CH_2)_3CH_3$

Scheme I.30



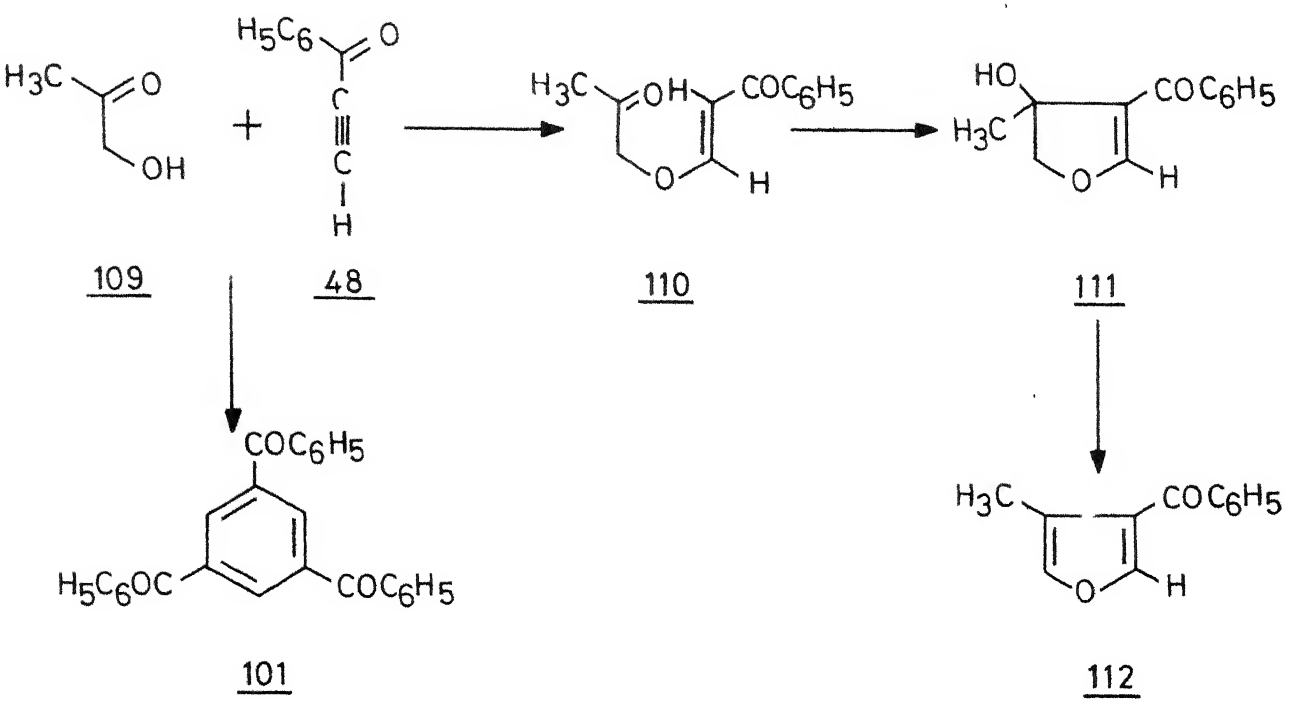
106 74 107 108

derivative 111, which subsequently undergoes elimination of water to give 112. The formation of 101, however, is understood in terms of the base-catalyzed trimerization of 48 (Scheme I.31).

The reactions of phenols, containing appropriate functional groups at the ortho-positions, with acetylenic ketones have been fairly well explored for the synthesis of heterocycles. Benzo-1,3-oxathiazoles, for example, are formed in the reaction of o-mercaptophenol (113) with acetylenic ketones.[110,112] Thus, the reaction of 113 with p-anisylbenzoylacetylene (114) gives rise to 2-phenacyl-2-(p-anisyl)-benzo-1,3-oxathiazole (116), the formation of which can be rationalized in terms of the intramolecular cyclization of the initially formed 1:1 adduct 115, as shown in Scheme I.32.[110,112] The reaction of catechol with acetylenic ketones has been reported to give 1:1 adducts in the absence of any catalysts, whereas in the presence of catalysts such as triethylamine[36] and potassium carbonate,[114] 1,3-benzodioxoles are formed.

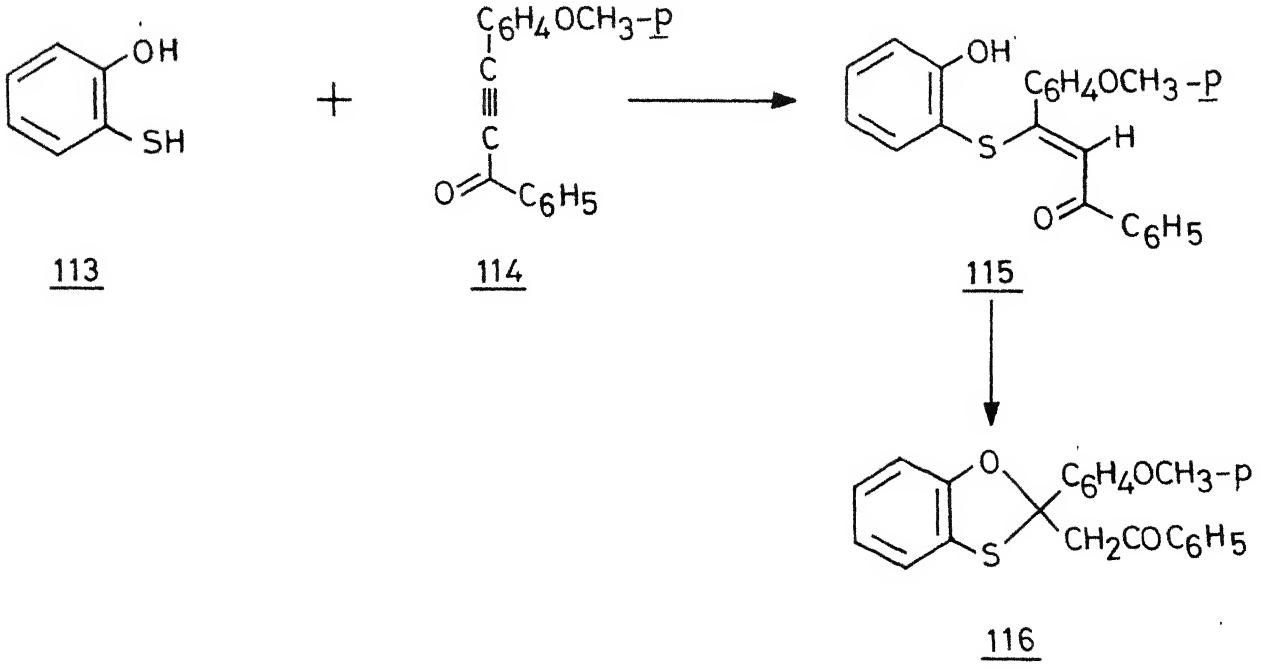
The reaction of o-hydroxycarboxylic acids with acetylenic ketones has been successfully employed for the synthesis of 1,3-dioxin-4-one derivatives.[36] For example, 2-hydroxy-3-naphthoic acid (117) reacts with benzoylacetylene (48) in the presence of triethylamine to form 2-phenacyl-4H-naphtho[2,3-d]-m-dioxin-4-one (119), whereas the reaction of

Scheme I.31



109 48 110 111 101 112

Scheme I.32



113 114 115 116

2-hydroxy-1-naphthoic acid (120) with 48 gives a mixture of products consisting of 2-phenacyl-1H-naphtho[2,1-d]-m-dioxin-1-one (121) and trans-3-β-naphthoxy-1-phenylprop-2-en-1-one (122) (Scheme I.33).[36]

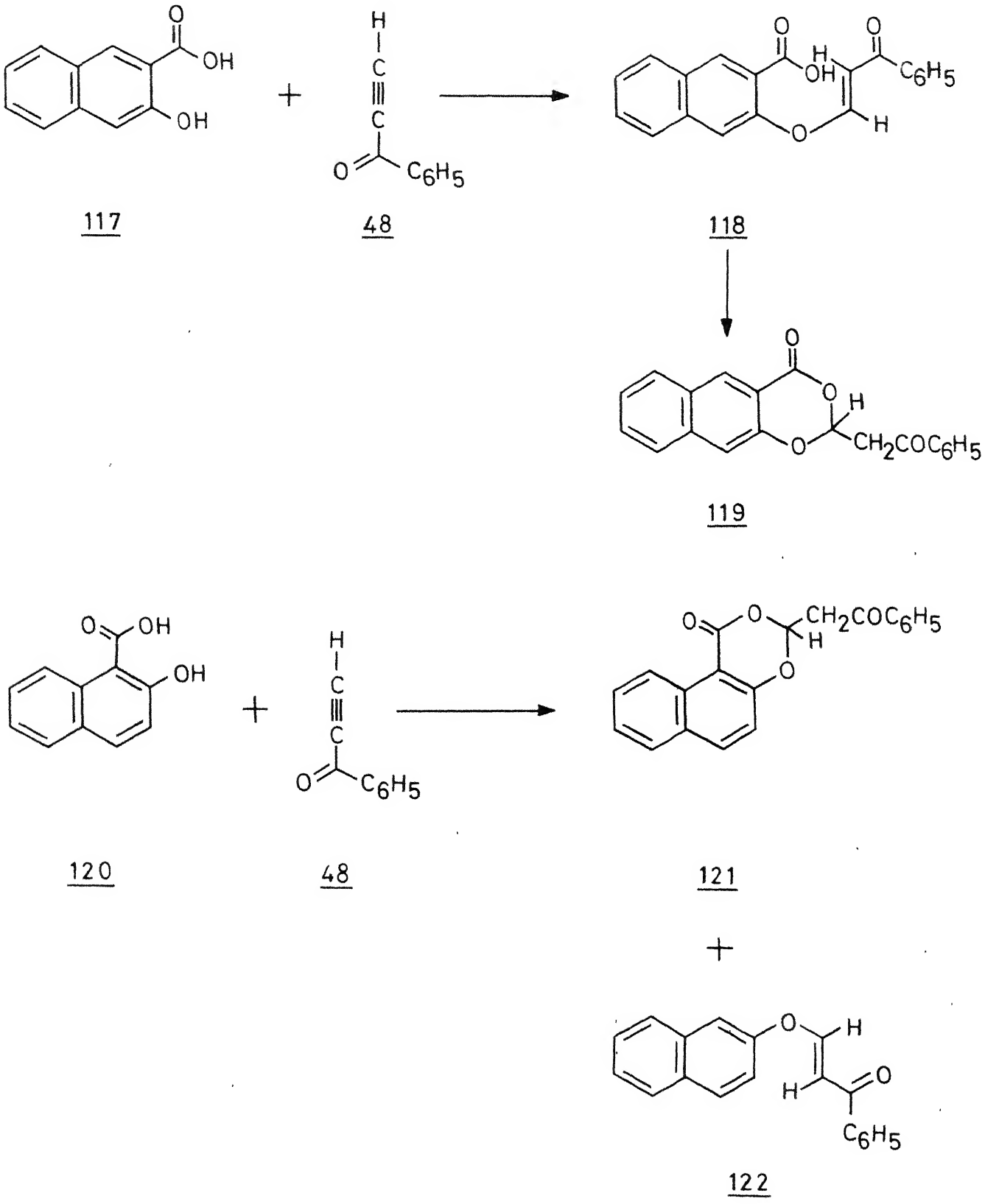
Salicylaldehyde (123) is known to react with benzoylacetylene (48) in the presence of sodium hydroxide to give 2-hydroxy-3-benzoylchrom-3-ene (124) (Scheme I.34), whereas in the presence of triethylamine, a complex mixture of products is formed.[36] An α-ketoalcohol such as benzoin (125) reacts with DBA, in the presence of potassium carbonate to form a dihydro furan derivative 128, which undergoes dehydration, under acidic conditions to give 2,3-dibenzoyl-4,5-diphenylfuran (127), as shown in Scheme I.35.[51,104]

I.4 SULFUR CONTAINING NUCLEOPHILES

I.4.1 Thiols and Thiophenols

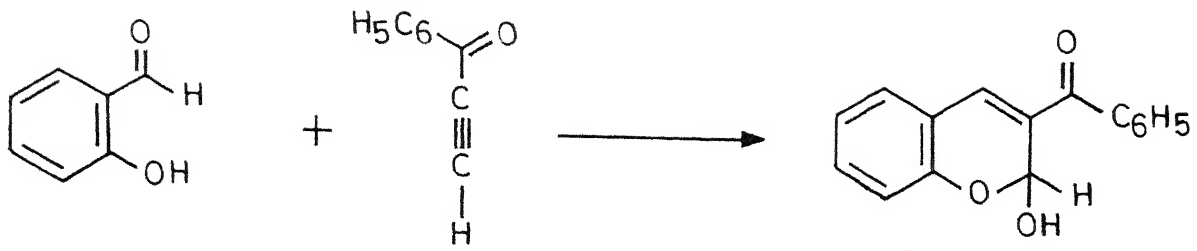
Similar to the reaction of phenols, mercaptans react with acetylenic ketones to give 1:1 adducts in the presence of different catalysts such as alkoxides,[3] piperidine,[3,115] sodium hydroxide[116] and triethylamine.[117] Omar and Basyouni[115] have shown that piperidine catalyses the addition of mercaptans to benzoyl and p-chlorobenzoylphenylacetylenes to give a mixture of 1:1 adducts consisting of both E- and Z-isomers, in each case, whereas Akiyama et al.[116] have shown that tert-butylmercaptan

Scheme I.33



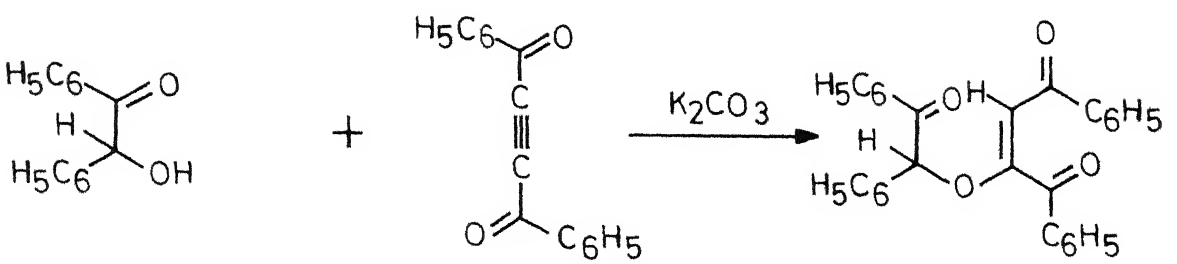
117 48 118 119 120 48 121 122

Scheme I.34

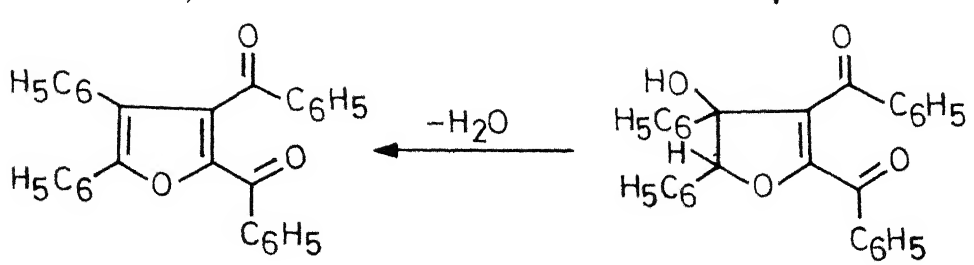


123 48 124

Scheme I.35



125 2 126



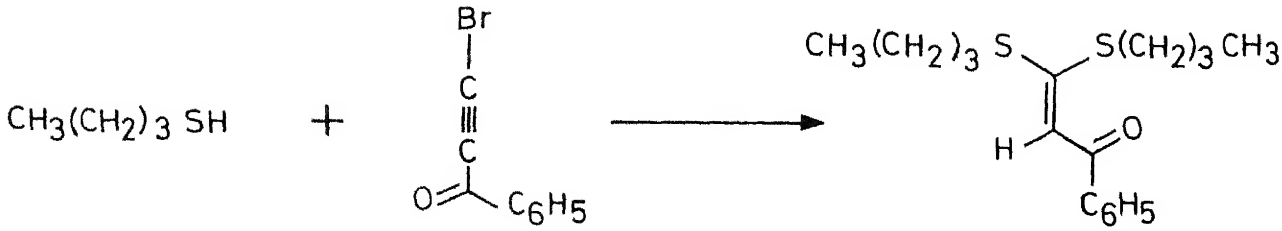
127 128

reacts with acetylacetylene, in the presence of sodium hydroxide to give a 1:1 adduct, primarily of the E-configuration. The reaction of mercaptans with an acetylenic ketone such as 1-benzoyl-2-bromoacetylene (130) is of interest in that both nucleophilic addition, as well as substitution occur in the same substrate. The reaction of n-butylmercaptan (129) with 130, for example, gives rise to 3,3-di-(n-butylmercapto)-1-phenylprop-2-en-1-one (131), as shown in Scheme I.36.[117]

It has been reported that alkyl mercaptans react with acetylacetylene in alcoholic solutions containing Triton B to give 1:1 adducts, which exists predominantly in the E-configuration.[118-120] When the reaction of alkyl mercaptans with acetylenic ketones is carried out in the presence of either tris(N,N-dimethylamino) phosphonium oxide or dimethylsulfoxide, the cis-trans isomerization has been found to be rapid, under the reaction conditions.[121] Mercaptans also add to α-hydroxyacetylenic ketones to give the corresponding 1:1 adducts.[122] Reports have also appeared in the literature concerning the formation of 1:2 adducts in the reaction of mercaptans with monosubstituted acetylenic ketones.[123]

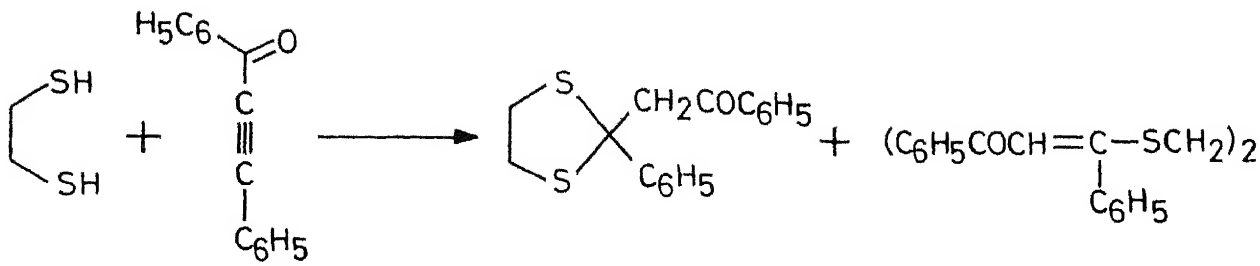
1,2-Dithiols are known to react with acetylenic ketones to give dithiolane derivatives. Thus, the reaction of 1,2-ethanedithiol (132) with benzoylphenylacetylene (74), for example, gives a mixture of the dithiolane derivative

Scheme I.36



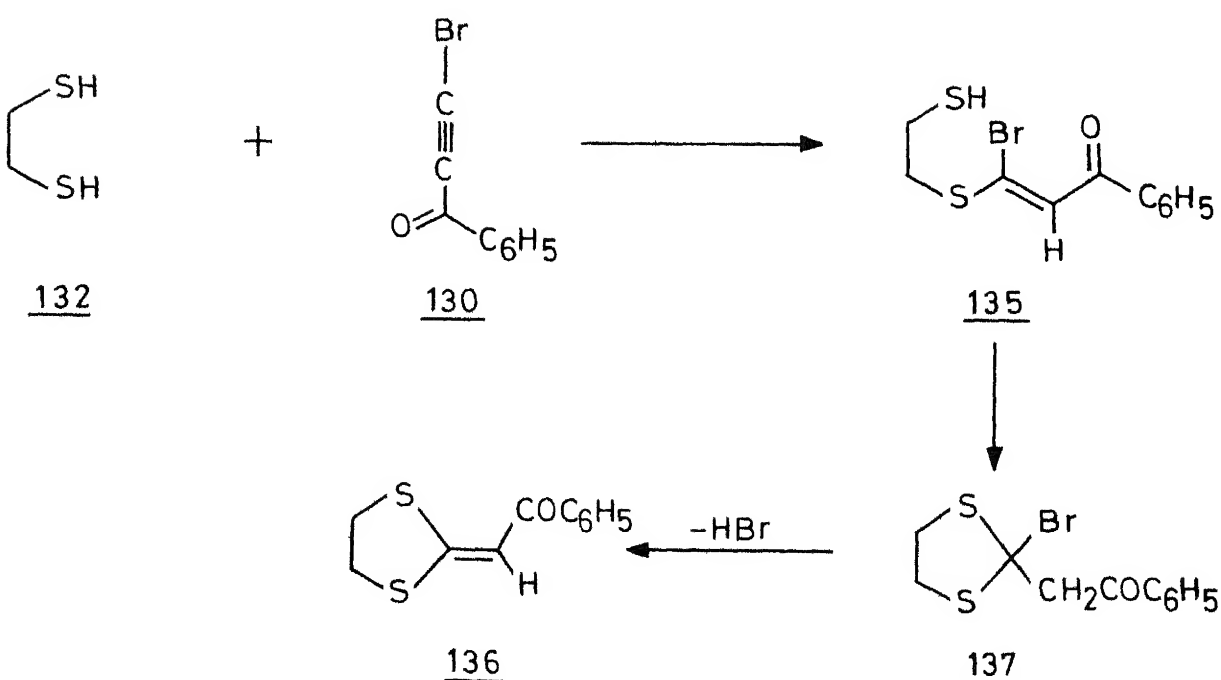
129 130 131

Scheme I.37



132 74 133 134

Scheme I.38



132 130 135 137 136

133 and the 1:2 adduct 134 (Scheme I.37).[124] Interestingly, the reaction of 132 with 1-benzoyl-2-bromoacetylene (130) gives 2-benzoylmethylene-1,3-dithiolane (136), formed through the loss of hydrogen bromide from the cyclized 1:1 adduct 137, as shown in Scheme I.38.[125]

Similar to the reactions of simple mercaptans, thiophenols add to acetylenic ketones to give the corresponding 1:1 adducts.[3,106,118,121,126-132] Basyouni and Omar[131] have observed that the pyridine-catalyzed addition of thiophenols to p-anisoylphenylacetylene in benzene yields a mixture of isomeric adducts of Z- and E-configuration, whereas in methanol or aqueous 1,4-dioxane, only the Z-isomer is obtained. Likewise, Nakhmanovich et al.[132] have shown that the reaction of thiophenol with acetylenic ketones in methanol and in the presence of triethylamine gives a mixture of both Z- and E-isomers of the 1:1 adducts.

Thiophenols, containing functional groups at ortho-positions react with acetylenic ketones to give sulfur containing heterocyclic compounds. o-Hydroxythiophenols, for example, react with acetylenic ketones to give the corresponding 1,3-benzoxathiazole derivatives.[110,112] Similarly, the reaction of 3,4-toluenedithiol (138) with benzoylphenylacetylene (74) gives 6-methyl-2-phenacyl-2-phenyl-1,3-benzodithiole (139)

(Scheme I.39).[133] Tripathi et al.[36] have observed that thiosalicylic acid (140) reacts with benzoylacetylene (48), in the presence of triethylamine to give 2-phenacyl-3,1-benzoxathiin-4-one (149), as shown in Scheme I.40

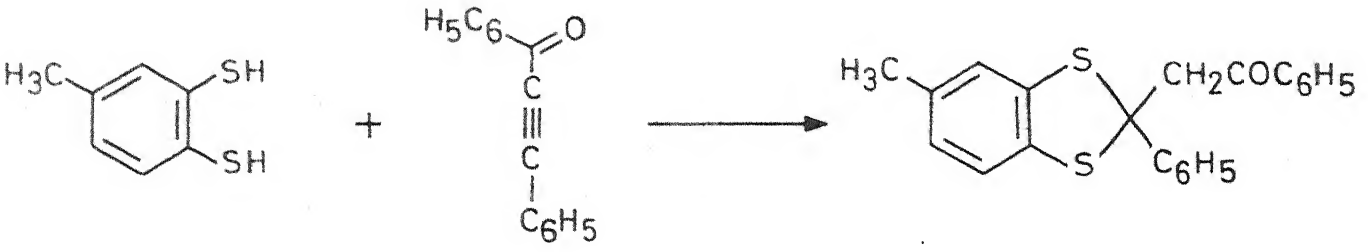
I.4.2 Thiones

Undheim and Riege[134] have observed that pyridine-2-thiones react with acetylenic ketones to form 1:1 adducts, having the E-configuration. The reaction of pyridine-2-thione (142) with acetylacetylene (64), for example, gives 4-(S-2-pyridino-thio)but-3-en-2-one (143), as shown in Scheme I.41. Similarly, indene-2-thiones react with acetylenic ketones to give the corresponding 1:1 adducts.[135]

I.4.3 Thiocarbamates

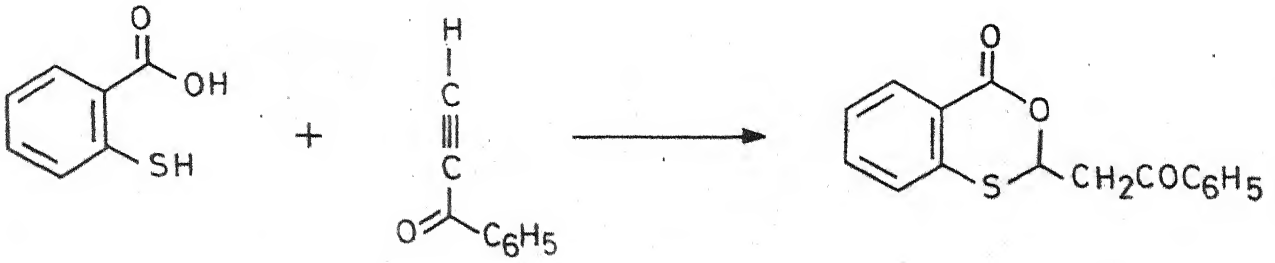
Baddar et al.[136] have shown that the reaction of ammonium dithiocarbamate (144) with acetylenic ketones gives rise to different products, depending on the reaction conditions. The reaction of 144 with aroylphenylacetylenes 145a-d in 60% aqueous dioxane at 15°, for example, gives a mixture of products consisting of the corresponding β-hydroxy-α-thiobenzoylstyrene derivatives, 151a-d and (E,Z)-β,β'-di-(α-aroylstyryl) sulfides 152a-d, in a 1:2 ratio (Scheme I.42). On the other hand, when the reaction of 144 with 145a was carried out in ethanol, a mixture of products, consisting of 151a and the (E,E) isomer of

Scheme I.39



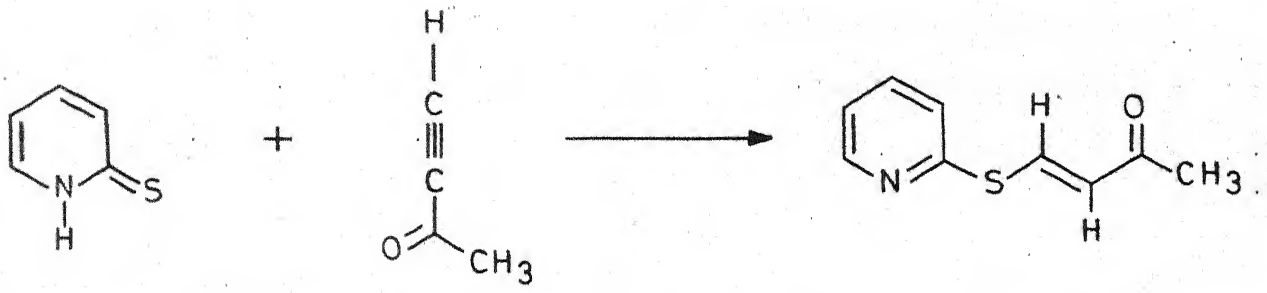
138 74 139

Scheme I.40



140 48 141

Scheme I.41



142 64 143

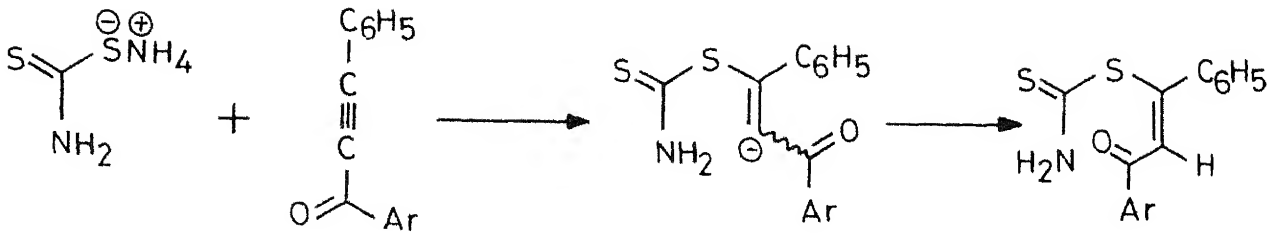
152a was obtained. Further, it has been shown that the (E,Z) isomer of 152a is converted to the corresponding (E,E) isomer, on refluxing in ethanol. Similar results have been obtained in the reaction of 144 with 145f. In contrast, the reaction of 144 with acetylenic ketones 145e,f in 60% aqueous dioxane, under analogous conditions, gives a mixture of 151e,f and small amounts of (E,E)-β,β'-di(α-aroylstyryl) disulfides [153e,f or 154e,f] (Scheme I.42).

The reaction of ammonium hydrogen sulfide with acetylenic ketones 145a-f, on the other hand, gives a mixture of 151a-f and 152a-f in a 1:2 ratio. However, strong nucleophiles such as sodium xanthate or sodium sulfide react with 145a-f to give the corresponding 1:1 adducts exclusively.

I.5 MISCELLANEOUS NUCLEOPHILES

Several other nucleophiles such as selenophenols,[137,138] and tellurophenols[137,139] have been treated with acetylenic ketones and, in general, the corresponding 1:1 adducts have been obtained. The reaction of chlorodiphenylphosphine with DBA has also been reported to give the corresponding addition product.[140]

Scheme 1.42



144 145 a , Ar = C_6H_5 146 147

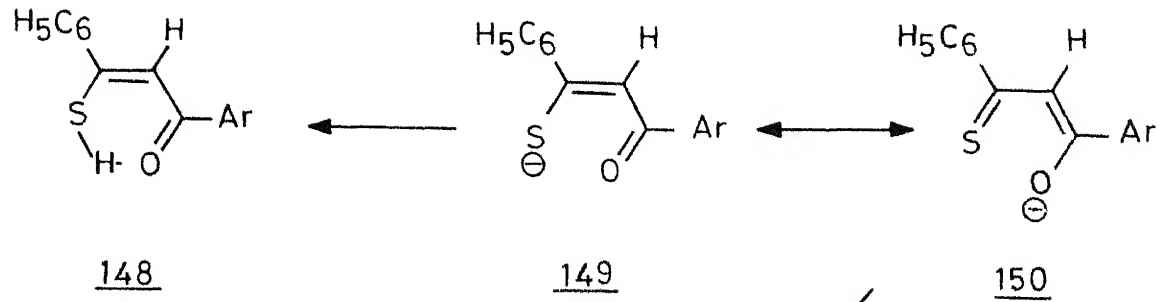
b , Ar = m-ClC_6H_4

c , Ar = p-$CH_3OC_6H_4$

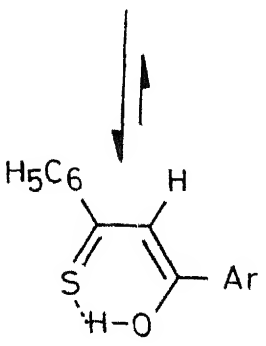
d , Ar = 3,4-$OCH_2OC_6H_3$

e , Ar = p-$CH_3C_6H_4$

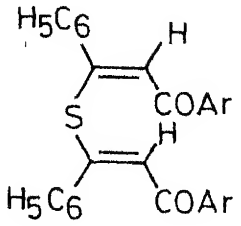
f , Ar = p-ClC_6H_4



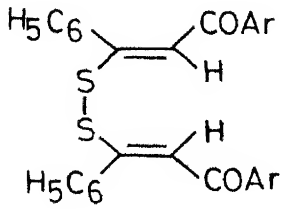
148 149 150



151

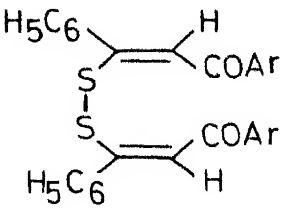


152



153

or



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I.6 REFERENCES

1. R. L. Bol'shedvorskaya and L. I. Vereshchagin, Russian Chem. Rev., 42, 225 (1973).

2. E. Andre', Compt. rend., 152, 525; Chem. Abstr., 5, 2092 (1911).

3. K. Bowden, E. A. Braude and E. R. H. Jones, J. Chem. Soc., 945 (1946).

4. I. Hirao, J. Chem. Soc. Japan, Ind. Chem. Sec., 57, 62 (1954); Chem. Abstr., 49, 3185 (1955).

5. E. Andre', Ann. Chim. Phys., 29, 540 (1913); Chem. Abstr., 7, 3490 (1913).

6. A. N. Grinev and V. I. Shvedov, Zhur. Obshch. Khim., 32, 2614 (1962); Chem. Abstr., 58, 7896 (1963).

7. V. Vidugiriene, Liet. TSR Mokslu Akad. Darb., Ser. B, 55 (1968); Chem. Abstr., 70, 28436 (1969).

8. Z. B. Alaune, Z. Talaikyte and G. Dienys, Liet. TSR Mokslu Akad. Darb., Ser. B, 65 (1968); Chem. Abstr., 70, 28569 (1969).

9. J. Reisch, Arch. Pharm., 298, 591 (1965); Chem. Abstr., 63, 16289 (1965).

10. R. L. Bol'shedvorskaya, S. P. Korshunov, S. I. Demina and L. I. Vereshchagin, Zhur Org. Khim., 4, 1541 (1968); Chem. Abstr., 70, 3983 (1969).

11. C. H. McMullen and C. J. M. Stirling, J. Chem. Soc. (B), 1221 (1966) and references cited therein.

12. G. Dupont, Bull. Soc. Chim. France, 41, 1167 (1927); Chem. Abstr., 22, 380 (1928).

13. J. Ballet, Bull. Soc. Chim. France, 41, 1170 (1927); Chem. Abstr., 22, 1767 (1928).

14. E. I. Titova, L. D. Gavrilov, R. L. Bol'shedvorskaya and L. I. Vereshchagin, Zhur. Org. Khim., 5, 2113 (1969); Chem. Abstr., 72, 66317 (1970).

15. R. E. Lutz, T. Amacker, S. M. King and N. H. Shearer, J. Org. Chem., 15, 181 (1950).

16. E. I. Titova, L. D. Gavrilov, T. N. Alesina and L. I. Vereshchagin, Izv. Nauch.-Issled. Inst. Nefte-Uglekhim. Sin. Irkutsk. Univ., 12, 33 (1970); Chem. Abstr., 75, 88253 (1971).

17. R. L. Bol'shedvorskaya, G. A. Pavlova, L. D. Gavrilov, N. V. Alekseeva and L. I. Vereshchagin, Zhur. Org. Khim., 8, 1879 (1972); Chem. Abstr., 78, 15707 (1973)

18. L. I. Vereshchagin, L. D. Gavrilov, E. I. Titova, S. R. Buzilova dnd R. L. Bol'shedvorskaya, Dokl., Vses. Konf. Khim. Atsetilena, 1, 364 (1972); Chem. Abstr., 79, 31019 (1973).

19. G. E. Hardtmann and F. G. Kathawala, Swiss Patent, 539,050 (1973); Chem. Abstr., 79, 115617 (1973).

20. M. F. Shostakovskii, Z. N. Deryagina and A. S. Nakhmanovich, Khim. Atsetilena, Tr. Vses. Konf., 3rd, 99 (1968); Chem. Abstr., 79, 18519 (1973).

21. E. V. Vasil'eva, E. M. Auvinen and I. A. Favorskaya, Zhur. Org. Khim., 11, 313 (1975); Chem. Abstr., 82, 124986 (1975).

22. L. I. Vereshchagin, R. L. Bol'shedvorskaya, G. A. Pavlova, A. A. Vereshchagina and N. V. Alekseeva, Zhur. Org. Khim., 11, 99 (1975); Chem. Abstr., 82, 85691 (1975).

23. N. V. Korzhova, V. S. Pisareva, L. V. Unikovskaya and S. P. Korshunov, Osnovn. Org. Sint. Neftekhim., 2, 99 (1975); Chem. Abstr., 83, 178024 (1975).

24. V. S. Pisareva, N. V. Korzhova, V. M. Kazantseva and S. P. Korshunov, Zhur. Org. Khim., 12, 1026 (1976); Chem. Abstr., 85, 45750 (1976).

25. N. V. Korzhova, V. S. Pisareva, O. M. Slyusareva and S. P. Korshunov, Zhur. Org. Khim., 13, 2555 (1977); Chem. Abstr., 88, 73823 (1978).

26. O. M. Slyusareva, V. S. Pisareva, S. P. Korshunov and V. M. Kazantseva, Zhur. Org. Khim., 13, 2285 (1977); Chem. Abstr., 88, 49931 (1978).

27. I. A. Favorskaya, E. M. Auvinen and E. V. Vasil'eva, Tezisy Dokl.-Vses. Konf. Khim. Atsetilena, 5th, 466 (1975); Chem. Abstr., 89, 42673 (1978).

28. O. M. Slyusareva, N. V. Korzhova and S. P. Korshunov, Zhur. Org. Khim., 14, 2258 (1978); Chem. Abstr., 90, 136964 (1979).

29. E. R. Watson, J. Chem. Soc., 1319 (1904).

30. K. Bowden, E. R. Braude, E. R. H. Jones and B. C. L. Weedon, J. Chem. Soc., 45 (1946).

31. K. Bowden and E. R. H. Jones, J. Chem. Soc., 953 (1946).

32. A. F. Popov, L. I. Kostenko, L. M. Litvinenko and A. A. Yakovets, Zhur. Org. Khim., 8, 2144 (1972); Chem. Abstr., 78, 57333 (1973)

33. V. S. Pisarera, N V. Korzhova, O. M. Slyusareva, M. G. Yartsev and S. P. Korshunov, Zhur. Org. Khim., 13, 350 (1977); Chem. Abstr., 87, 21862 (1977)

34. E. N. Deryagina, A. S. Nakhmanovich, V. I. Knutov, I. D. Kalikhman and E. I. Kositsina, Izv. Sib. Otd. Akad Nauk SSSR, Ser. Khim. Nauk 1, 118 (1977); Chem. Abstr., 87, 22913 (1977).

35. S. Lahiri, M. P. Mahajan, R. Prasad and M. V. George, Tetrahedron, 33, 3159 (1977)

36. V. K. Tripathi, P. S. Venkataramani and G. Mehta, J. Chem. Soc. Perkin I, 36 (1979).

37. L. I. Vereshchagin, E. I. Titova, T. V. Lipovich and L. D. Gavrilov, Zhur. Org. Khim., 7, 903 (1971); Chem. Abstr., 75, 63317 (1971).

38. N. V. Korzhova, V. S. Pisareva and S. P. Korshunov, Zhur. Org. Khim., 11, 1030 (1975); Chem. Abstr., 83, 78046 (1975).

39. N. V. Korzhova and S. P. Korshunov, Fiz.-Khim. Izuch. Neorgan. Soedin, 4, 100 (1976); Chem. Abstr., 87, 21857 (1977).

40. O. H. Hankovszky, K. Hideg and D. Lloyd, J. Chem Soc. Perkin I, 1619 (1974).

41. L. I. Vereshchagin, L. D. Gavrilov and R. L. Bol'shedvorskaya, Zhur. Org. Khim., 10, 2059 (1974); Chem. Abstr., 82, 43338 (1975).

42. L. I. Vereshchagin, E. I. Titova, L. G. Tikhonova, S. R. Buzilova, L. D. Gavrilov and G. A. Kalabin, Zhur. Org. Khim., 10, 978 (1974); Chem. Abstr., 81, 63437 (1974).

43. L. G. Tikhonova, E. I. Titova, L. D. Gavrilov, L. L. Okhapina and L. I. Vereshchagin, Tezisy Dokl.-Vses. Konf. Khim. Atsetilena, 5th, 293 (1975); Chem. Abstr., 89, 24740 (1978).

44. L. G. Tikhonova, E. I. Titova, L. D. Gavrilov, L. I. Vereshchagin and A. G. Praidakov, Zhur. Org. Khim., 11, 2510 (1975); Chem. Abstr., 84, 105327 (1976).

45. A. P. Bindra and E. LeGoff, Tetrahedron Lett., 1523 (1974).

46. W. Ried and E. Koenig, Justus Liebigs Ann. Chem., 24 (1972); Chem. Abstr., 76, 140748 (1972).

47. S. P. Korshunov, V. M. Kazantseva, L. A. Vopilina, V. S. Pisareva and N. V. Utekhina, Khim. Geterotsikl. Soedin., 1421 (1973); Chem. Abstr., 80, 27225 (1974).

48. R. G. Bass, D. D. Crichton, H. K. Meetz and A. F. Johnson, Tetrahedron Lett., 2073 (1975)

49. R. L. Amey and N. D. Heindel, Org. Prep. Proced. Int., 8, 306 (1976); Chem. Abstr., 86, 155623 (1977).

50. W. Ried and R. Teubner, Justus Liebigs Ann. Chem., 741 (1978); Chem. Abstr., 89, 109402 (1978)

51. S. E. Drewes and P. C. Coleman, Chem. Ind. (London), 22, 995 (1976).

52. K. T. Potts and A. J. Elliott, J. Org. Chem., 38, 1769 (1973).

53. V. Vesa and G. Kupetis, Liet. TSR Mokslu Akad. Darb. Ser. B, 89 (1967); Chem. Abstr., 68, 39167 (1968).

54. L. I. Vereshchagin, L. P. Kirillova, S. R. Buzilova, R. L. Bol'shedvorskaya and G. V. Chernysheva, Zhur. Org. Khim., 11, 531 (1975); Chem. Abstr., 83, 28136 (1975).

55. L. I. Vereshchagin, A. G. Proidakov, L. D. Gavrilov and G. A. Kalabin, Zhur. Org. Khim., 15, 699 (1979), Chem. Abstr., 91, 74101 (1979).

56. M. G. Voronkov, V. I. Knutov, L. M. Chudesova and O. B. Bannikova, Khim. Geterotsikl. Soedin., 55 (1979); Chem. Abstr., 90, 203781 (1979).

57. R. Fusco, G. Bianchetti, D. Pocar and R. Ugo, Gazz. Chim. Ital., 92, 1040 (1962).

58. T. Cuvigny and H. Normant, Compt. rend., 247, 1744 (1958); Chem. Abstr., 53, 12164 (1959).

59. C. Lutz, Chem. Ber., 91, 1867 (1958).

60. H. W. Heine, T. R. Hoye, P. G. Willard and R. C. Hoye, J. Org. Chem., 38, 2984 (1973).

61. S. P. Korshunov, N. A. Kudryavtseva, G. V. Frolova and N. V. Korzhova, Khim. Elementoorg. Soedin., Polim., 1-2, 45 (1972); Chem. Abstr., 81, 168824 (1974).

62. E. V. Vasil'eva, E. M. Auvinen and I. A. Favorskaya, Zhur. Org. Khim., 14, 1602 (1978); Chem. Abstr., 89, 163206 (1978).

63. V. S. Pisareva, N. V. Korzhova, V. M. Kazantseva and S. P. Korshunov, Zhur. Org. Khim., 11, 1034 (1975); Chem. Abstr., 83, 78047 (1975).

64. O. M. Slyusareva, N. V. Korzhova and S. P. Korshunov, Zhur. Org. Khim., 13, 1015 (1977); Chem. Abstr., 87, 52605 (1977).

65. N. V. Korzhova, V. S. Pisareva, O. M. Slyusareva, V. M. Kazantseva and S. P. Korshunov, Zhur. Org. Khim., 11, 2255 (1975); Chem. Abstr., 84, 43083 (1976).

66. V. S. Pisareva, N. V. Korzhova, V. A. Minaeva, V. M. Kazantseva and S. P. Korshunov, Zhur. Org. Khim., 10, 1900 (1974); Chem. Abstr., 82, 16167 (1975).

67. C. J. Cavallito, J. Am. Chem. Soc., 77, 4159 (1955).

68. G. W. Fischer, Z. Chem., 8, 269 (1968); Chem. Abstr , 69, 58914 (1968).

69. H. J. Gais, K. Hafner and M. Neuenschwander, Helv. Chim. Acta, 52, 2641 (1969).

70. L. I. Vereshchagin, S. P. Korshunov, V. I. Skoblikova and T. V. Lipovich, Zhur. Org. Khim., 1, 1089 (1965); Chem. Abstr , 63, 11536 (1965).

71. K. Schlögl and A. Mohar, Monatsh., 93, 861 (1962); Chem. Abstr., 59, 3950 (1963).

72. I. I. Lapkin and Yu. S. Andreichikov, Zhur. Org. Khim., 2, 2075 (1966); Chem. Abstr., 66, 75947 (1967).

73. G. Coispeau and J. Elguero, Bull. Soc. Chim. France, 2717 (1970).

74. N. R. El-Rayyes and F. H. Al-Hajjar, J. Heterocyclic Chem., 14, 367 (1977).

75. E. R. H. Jones, T. Y. Shen and M. C. Whiting, J. Chem. Soc., 236 (1950).

76. A. S. Nakhmanovich, V. N. Elokhina, L. V. Timokhina and M. G. Voronkov, Tezisy Dokl.-Vses. Konf. Khim. Atsetilena, 5th, 370 (1975); Chem. Abstr., 89, 59811 (1978)

77. L. I. Vereshchagin, L. D. Gavrilov, E. I. Titova, S. R. Buzilova, N. V. Sushkova and A. V. Maksikova, Zhur. Org. Khim., 11, 47 (1975); Chem. Abstr., 82, 139997 (1975)

78. A. Engelmann and W. Kirmse, Chem. Ber., 106, 3092 (1973).

79. F. G. Baddar, F. H. Al-Hajjar and N. R. El-Rayyes, J. Heterocyclic Chem., 15, 385 (1978).

80. Y A. Al-Farkh, F. H. Al-Hajjar and H. S. Hamoud, Chem. Pharm. Bull., 26, 1298 (1978).

81. F. H. Al-Hajjar, El-Ezaby, S. Mohamed, N. R. El-Rayyes and R. Nizar, Chem. Pharm. Bull., 25, 548 (1977).

82. R. W. Fries, D. P. Bohlken and B. V. Plapp, J. Med. Chem., 22, 356 (1979).

83 F. G. Baddar, F. H. Al-Hajjar and N. R. El-Rayyes, J. Heterocyclic Chem., 13, 257 (1976).

84. W. Sucrow and M. Slopianka, Chem. Ber., 105, 3807 (1972)

85. V. Bardakos, W. Sucrow and A. Fehlauer, Chem. Ber., 108, 2161 (1975).

86. K. M. Johnston and R. G. Shotter, J. Chem. Soc. (C), 1774 (1968).

87. D. Nightingale and F. Wadsworth, J. Am. Chem. Soc., 67, 416 (1945).

88. C. Weygand, E. Bauer and W. Heynemann, Ann. 459, 123 (1927); Chem. Abstr., 22, 1159 (1928).

89. L. Birkofer and K. Richtzenhain, Chem. Ber., 112, 2829 (1979)

90. H. Bredereck, R. Gompper and G. Morlock, Chem. Ber., 91, 2830 (1958).

91. C. Barat, J Indian Chem. Soc., 7, 851 (1930).

92. F. H. Al-Hajjar and A. A. Jarrar, J. Heterocyclic Chem., 17, 1521 (1980).

93. French Patent 1,522,696 (1968); Chem. Abstr., 71, 81405 (1969).

94. G. E. Hardtmann and F. G. Kathawala, Swiss Patent 539,049 (1973); Chem. Abstr., 79, 115616 (1973).

95. F. G. Baddar, F. H. Al-Hajjar and N. R. El-Rayyes, J. Heterocyclic Chem., 15, 105 (1978).

96. R. E. Rosenkranz, K. Allner, R. Good, W. v. Philipsborn and C. H. Eugster, Helv. Chim. Acta, 46, 1259 (1963).

97. F. Bohlmann and D. Rahtz, Chem. Ber., 90, 2265 (1957).

98. C. L. Bickel, J. Am Chem. Soc., 71, 336 (1949).

99. C. L. Bickel, J. Am. Chem. Soc., 69, 73 (1947).

100. C. Moureu and M. Brachin, Bull. Soc. Chim. France, 33, 131 (1905).

101. C. Moureu and R. Deluge, Compt. rend., 130, 1259 (1900).

102. L. I. Vereshchagin, N. V. Sushkova, S. R. Buzilova and E. I. Titova, Dokl. Vses. Konf. Khim. Atsetilena, 1, 173 (1972); Chem. Abstr., 79, 91901 (1973).

103. L. I. Vereshchagin, N. V. Sushkova, S. R. Buzilova, L. P. Kirillova and S. I. Demina, Zhur. Org. Khim., 11, 286 (1975); Chem. Abstr., 82, 155211 (1975)

104. L. I. Vereshchagin, R. L. Bol'shedvorskaya, A. V. Maksikova, L. G. Tikhonov and E. I. Titova, Zhur. Org. Khim., 13, 1836 (1977); Chem. Abstr., 88, 22296 (1978).

105. J. S. Walia and A. S. Walia, J. Org. Chem., 41, 3765 (1976).

106. P. E. Eaton and C. E. Stubbs, J. Am. Chem. Soc., 89, 5722 (1967).

107. M. F. Shostakovskii, N. V. Komarov and V. B. Pukhnarevich, Zhur. Obshch. Khim., 38, 1172 (1968); Chem. Abstr., 69, 77323 (1968).

108. P. S. Venkataramani, N. K. Saxena, V. K. Tripathi and G. Mehta, Indian J. Chem., 852 (1975).

109. V. N. Elokhina, A. S Nakhmanovich and M. G. Voronkov, Tezisy Dokl.-Simp. Khim. Tekhnol. Geterotsikl. Soedin. Goryuch. Iskop., 2nd, 110 (1973), Chem. Abstr., 86, 29556 (1977).

110. V. N. Elokhina, A. S. Nakhmanovich, I. D. Kalikhman and M. G. Voronkov, Tezisy Dokl.-Vses. Konf. Khim. Atsetilena, 5th, 298 (1975); Chem. Abstr., 88, 170015 (1978).

111. A. S. Nakhmanovich, V. N. Elokhina, I. D. Kalikhman and M. G. Voronkov, Khim. Geterotsikl. Soedin., 8, 1041 (1978); Chem. Abstr., 90, 6282 (1979).

112. V. N. Elokhina, A. S. Nakhmanovich, I. D. Kalikhman, N. P. Sokol'nikova and M. G. Voronkov, Khim. Geterotsikl. Soedin., 1328 (1975); Chem. Abstr., 84, 43912 (1976).

113. E. Manghisi and A. Salimbeni, Ger. Patent, 2,502,938 (1975); Chem. Abstr., 83, 147303 (1975).

114. V Rosnati and A. Salimbeni, Gazz. Chim. Ital., 107, 271 (1977); Chem. Abstr., 88, 104306 (1978).

115. M. T. Omar and M. N. Basyouni, Bull. Chem. Soc. Japan, 47, 2325 (1974).

116. S. Akiyama, S. Nakatsuji, T. Hamamura, M. Kataoka and M. Nakagawa, Tetrahedron Lett., 2809 (1979).

117. A. S. Nakhmanovich, V. N. Elokhina, E. I. Kositsina and M. G. Voronkov, Izv Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk, 127 (1978); Chem. Abstr., 89, 108893 (1978).

118. E. N. Prilezhaeva, G. S. Vasil'ev, I. L. Mikhelashvili and V. S. Bogdanov, Zhur. Org. Khim., 7, 1349 (1971); Chem. Abstr., 75, 129023 (1971).

119. V. S. Bogdanov, I. L. Mikhelashvili and E. N. Prilezhaeva, Izv. Akad. Nauk SSSR, Ser. Khim., 2374 (1972); Chem. Abstr., 78, 28756 (1973).

120. I. L. Mikhelashvili-Fiolitya, V. S. Bogdanov, N. D. Chuvylkin and E. N. Prilezhaeva, Izv. Akad. Nauk SSSR, Ser. Khim., 890 (1975); Chem. Abstr., 83, 27378 (1975).

121. E. N. Prilezhaeva, I. L. Mikhelashvili, V. S. Bogdanov and G. S. Vasil'ev, Dokl. Vses. Konf. Khim. Atsetilena, 1, 525 (1972); Chem. Abstr., 79, 17699 (1973).

122. A. S. Mendvedeva, L. P. Safronova and M. G. Voronkov, Izv. Akad. Nauk SSSR, Ser. Khim., 1669 (1973); Chem. Abstr., 79, 104695 (1973).

123. E. N. Prilezhaeva and I. L. Mikhelashvili, Zhur. Org. Khim., 9, 1129 (1973); Chem. Abstr., 79, 78306 (1973).

124. V. N. Elokhina, R. V. Karnaukhova, A. S. Nakhmanovich, I. D. Kalikhman and M. G. Voronkov, Zhur. Org. Khim , 15, 57 (1979); Chem. Abstr., 91, 5133 (1979).

125. A. S. Nakhmanovich, V N. Elokhina, I. D Kalikhman and M. G. Voronkov, Khim. Geterotsikl. Soedin., 1137 (1977); Chem. Abstr., 87, 201390 (1977).

126. D. Landini and F. Montanari, Chem. Commun., 180 (1967).

127. W. E. Truce and R. F. Heine, J. Am. Chem. Soc., 79, 5311 (1957).

128. W. E. Truce and G. J. W. Tichenor, J. Org. Chem., 37, 2391 (1972).

129. A. S. Nakhmanovich, E. N. Deryagina and V. N. Elokhina, Khim. Geterotsikl. Soedin., Sb. 3, 45 (1971); Chem. Abstr., 78, 71809 (1973).

130. V. E. Statsyuk, S. P. Korshunov, N. V. Korzhova and I. V. Bodrikov, Zhur. Org. Khim., 15, 1998 (1979); Chem. Abstr., 92, 93567 (1980).

131. M. N. Basyouni and M. T. Omar, Egypt. J. Chem., 18, 469 (1975) (Pub. 1977).

132. A. S. Nakhmanovich, E. N. Deryagina and M. G. Voronkov, Dokl. Vses. Konf. Khim. Atsetilena, 2, 449 (1972); Chem. Abstr., 79, 126195 (1973).

133. M. N. Basyouni, M. T. Omar and E. A. Ghali, Synthesis, 115 (1980).

134. K. Undheim and L. A. Riege, J. Chem. Soc. Perkin I, 1493 (1975).

135. N. A. Korchevin, V. N. Elokhina, V. A. Usov and M. G. Voronkov, Tezisy Dokl.-Vses. Konf. Khim., Atsetilena, 5th, 328 (1975); Chem. Abstr., 89, 6037 (1978).

136. F. G. Baddar, F. H. Al-Hajjar and N. R. El-Rayyes, J. Heterocyclic Chem., 13, 691 (1976).

137. S. R. Buzilova, I. D. Sadekov, T. V. Lipovich, T. M. Filippova and L. I. Vereshchagin, Zhur. Obsch. Khim., 47, 1999 (1977); Chem. Abstr., 88, 22289 (1978).

138. A. K. Pasatev, Vestn. Akad. Nauk Kaz. SSR 70 (1977); Chem. Abstr., 87, 38714 (1977).

139. S. R. Buzilova, L. I. Vereshchagin, I. D. Sadekov and V. I. Minkin, Zhur. Obshch. Khim., 46, 932 (1976); Chem. Abstr., 85, 20761 (1976).

140. E. Fluck and W. Kazenwadel, Phosphorous, 6, 195 (1976); Chem. Abstr., 86, 88645 (1977).

Treatment of 13 with either HCl in methanol or with orthophosphoric acid gave a nearly quantitative yield (~95%) of 5-benzoyl-3-phenylpyrazole (17). Similarly, the reaction of benzoylphenylhydrazine (18) with DBA in methanol gave a 89% yield of 2-(2'-benzoyl-1'-phenylhydrazo)-1,4-diphenylbut-2-ene-1,4-dione (20). An attempted cyclization of 20 by treatment with orthophosphoric acid gave a 80% yield of 5-benzoyl-1,3-diphenylpyrazole (24), along with a 70% yield of benzoic acid. The reaction of ethyl N,C-diphenylglycinate (25) with DBA, on the other hand, gave a 90% yield of the cyclized pyrrole derivative, namely, 2,3-dibenzoyl-4-hydroxy-1,5-diphenylpyrrole (27).

In continuation of our studies, we have examined the reactions of a few hydrazones such as benzaldehyde hydrazone (29a), benzophenone hydrazone (29b), benzaldehyde phenylhydrazone (34a) and p-anisaldehyde phenylhydrazone (34b) with DBA. The reaction of 29a with DBA in methanol, for example, gave a 1:1 adduct, 2-(1'-hydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (31a, 88%), whereas 29b, under analogous conditions gave a 93% yield of 2-(1'-hydrazinyl-2'-benzhydrylidene)-1,4-diphenylbut-2-ene-1,4-dione (31b). The reaction of 34a with DBA, on the other hand, gave a mixture of products consisting of 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (39a, 19%) and 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (38, 8%). Similar products have been obtained in the

reaction of 34b with DBA. The reaction of benzil monohydrazone (40a) with DBA in refluxing xylene, on the other hand, gave a 91% yield of 3,4-dibenzoyl-5,6-diphenylpyridazine (45). Treatment of 45 with hydrazine resulted in the formation of 3,4,5,8-tetraphenylpyridazino[4,5-c]pyridazine (46, 68%).

The reaction of a diamine nucleophile such as ethylenediamine (47) with DBA has been shown to give a mixture of products consisting of 2-(2'-oxo-2'-phenylethylidene)-3-phenyl-1,2,5,6-tetrahydropyrazine (51, 69%) and N,N'-bis-(2'-(1',4'-diphenylbut-2'-ene-1',4'-dione))-1,2-diaminoethane (52, 31%). Reasonable mechanisms have been suggested to account for the formation of the different products in these reactions.

II.2 INTRODUCTION

Numerous reactions of nitrogen containing nucleophiles such as hydrazides, hydrazones and other related systems with acetylenic ketones are reported in the literature.[1] Hydrazides, in general, react with acetylenic ketones to give N-acyl or N-aroylhydrazones.[2-4] It has been observed that in the reaction of hydrazides (1a-d) with different acetylenic ketones (2a-d), for example, 1:1 adducts (5) are formed initially, which undergo cyclization either under basic or acidic conditions to give pyrazoles (4).[2-4] Treatment of the 1:1 adducts (5), with a

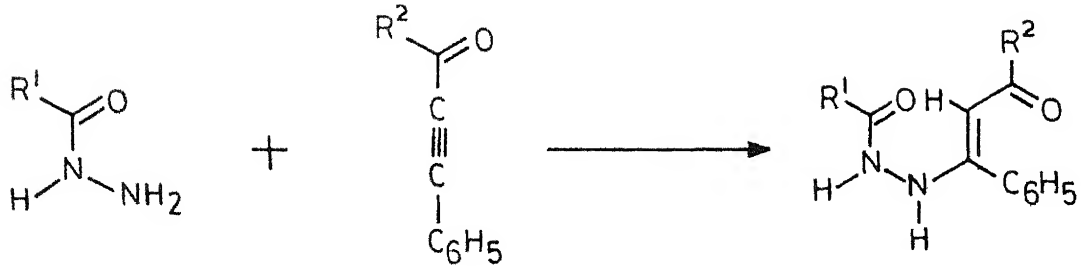
mixture of acetic anhydride and sodium acetate, on the other hand, results in the formation of the corresponding N-acetylated pyrazoles (6) (Scheme II.1).

The reaction of α-amino acid esters with acetylenic ketones has been reported to give a mixture of 1:1 and 1:2 adducts.[5,6] Also, it has been observed that furan derivatives are formed through the reactions of α-amino acid esters with either γ- or δ-hydroxyacetylenic ketones.[5,6]

The reactions of aldehyde and ketone hydrazones (7a-f) with acetylenic ketones (8) are shown to give ene-hydrazones (9a-f) (Scheme II.2).[7-9] On the basis of NMR studies, it has been shown that these adducts have the E-configuration, as far as their stereochemistry across the carbon-carbon double bond is concerned.

The object of the present investigation has been to examine the reactions of a few hydrazides, phenylhydrazides, hydrazones and phenylhydrazones and also ethylenediamine with DBA, with a view to understanding the nature of the products formed in these reactions and also to examine whether these reactions could be used for the synthesis of different heterocycles.

Scheme II.1

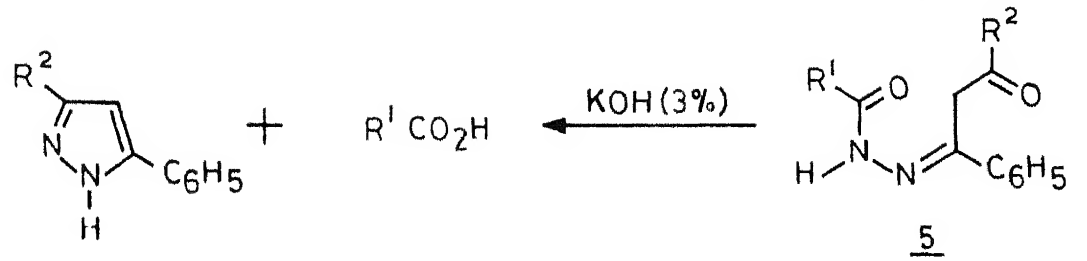


1a, $R^1 = C_6H_5$ 2a, $R^2 = C_6H_5$ 3

b, $R^1 = C_6H_5CH_2$ b, $R^2 = \underline{p}\text{-}CH_3C_6H_4$

c, $R^1 = \alpha\text{-}C_{10}H_7$ c, $R^2 = \underline{p}\text{-}ClC_6H_4$

d, $R^1 = \alpha\text{-}C_{10}H_7CH_2$ d, $R^2 = \underline{p}\text{-}CH_3OC_6H_4$



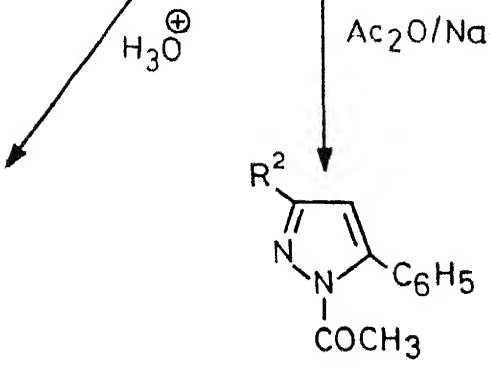
5

4a, $R^2 = C_6H_5$

b, $R^2 = \underline{p}\text{-}CH_3C_6H_4$

c, $R^2 = \underline{p}\text{-}ClC_6H_4$

d, $R^2 = \underline{p}\text{-}CH_3OC_6H_4$



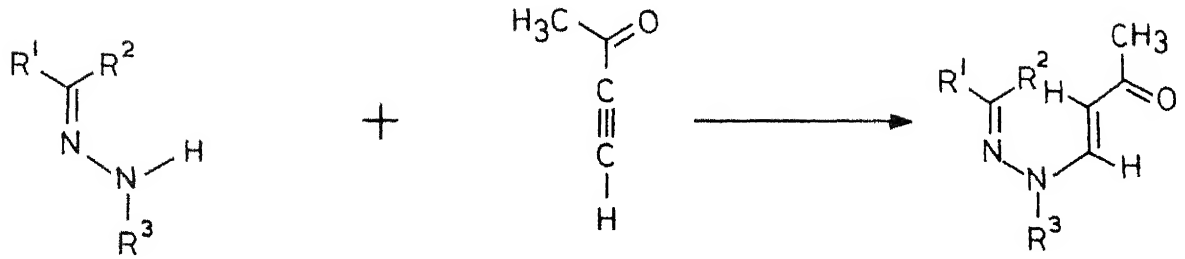
4 + R^1CO_2H

6a, $R^2 = C_6H_5$

b, $R^2 = \underline{p}\text{-}CH_3C_6H_4$

c, $R^2 = \underline{p}\text{-}ClC_6H_4$

Scheme II.2



7a, $R^1 = CH_3, R^2 = H, R^3 = C_2H_5$ 8 9a-f

b, $R^1 = C_2H_5, R^2 = H, R^3 = n\text{-}C_3H_7$

c, $R^1 = CH_3, R^2 = H, R^3 = CH(CH_3)_2$

d, $R^1, R^2 = -(CH_2)_4-$; $R^3 = CH_3$

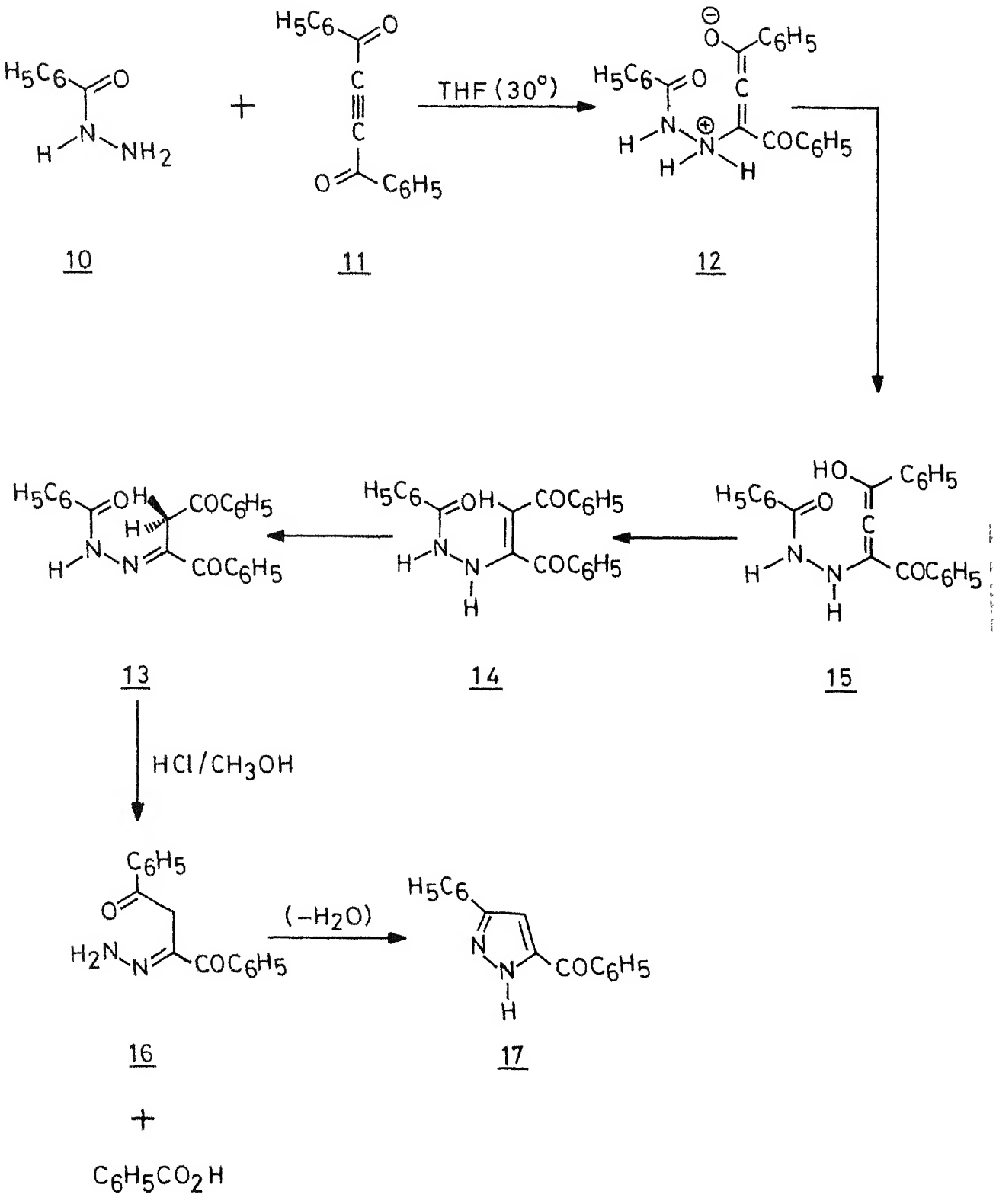
e, $R^1 = R^2 = R^3 = CH_3$

f, $R^1 = R^2 = CH_3$; $R^3 = CH(CH_3)_2$

II.3 RESULTS AND DISCUSSION

The reaction of benzoylhydrazine (10) with DBA in THF at room temperature gave a 92% yield of a product, identified as 2-(2'-benzoylhydrazono)-1,4-diphenylbutan-1,2,4-trione (13) (Scheme II.3). The structure of 13 has been established on the basis of analytical data, spectral information and chemical evidences. The IR spectrum of 13, for example, showed an NH band at 3444 cm^{-1} and two carbonyl absorptions at 1664 and 1644 cm^{-1}, respectively. Through concentration dependent IR studies in carbon tetrachloride solution, it has been observed that 13 exhibits a weak intermolecular hydrogen-bonding. The NMR spectrum of 13 (Fig. II.1) showed an AB type of quartet centred around δ 3.58 (J = 19 Hz), which has been assigned to the magnetically nonequivalent methylene protons. It is probable that the magnetic nonequivalence of the methylene protons is due either to the large anisotropic effect of the C=N group and the nitrogen lone pair or to the restricted rotation of the $CH_2COC_6H_5$ group due to the hydrogen-bonding between the NH and CO groups. It might be mentioned in this connection that analogous products having magnetically nonequivalent protons have been observed in the reaction of a few aroylhydrazines with acetylenic monoketones, and the reported chemical shift and coupling constant values for these compounds are in agreement with our observations.[2-4] Other

Scheme II.3



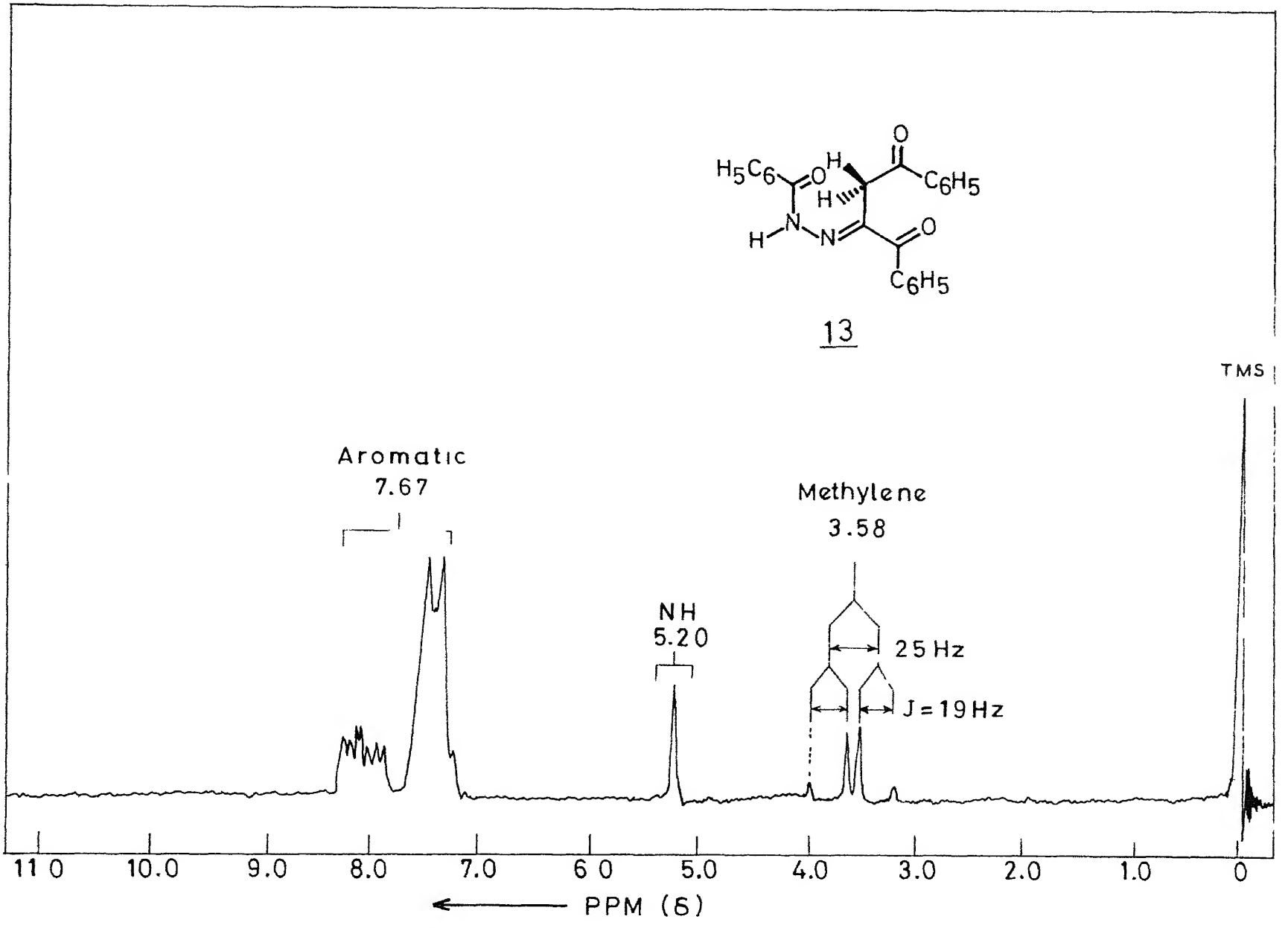


Fig II.1 NMR spectrum (60 MHz) of 13.

signals in the NMR spectrum of 13 were observed at δ 5.20 (1 H) and 7.67 (15 H). Of these, the signal at δ 5.20 was exchangeable with D_2O and has been assigned to the NH proton, whereas, the multiplet centred around δ 7.67 has been assigned to the aromatic protons.

The mass spectrum of 13 (Fig. II.2) showed a molecular ion peak at m/e 370 (1). Other peaks in the spectrum were observed at m/e 279 (1), 265 (3), 237 (2), 222 (2), 167 (5), 149 (13), 132 (2), 105 (85), 104 (5), 77 (100) and 51 (13). Some of the possible modes of fragmentation are shown in Scheme II.4.

Further evidence concerning the structure of 13 has been derived through its transformations, under acid-catalysed conditions. Treatment of 13 with methanolic hydrochloric acid under refluxing conditions, for example, gave a 70% yield of benzoic acid and a 95% yield of 5-benzoyl-3-phenylpyrazole (17). Similarly, treatment of 13 with orthophosphoric acid around 100° gave a 65% yield of benzoic acid and a 90% yield of 17.

The formation of 13 in the reaction of benzoylhydrazine (10) with DBA and its subsequent transformation to the pyrazole 17, under acid-catalysed conditions, can be explained in terms of the pathways shown in Scheme II.3. It has been assumed that the reaction of 10 with 11 gives rise initially to the zwitterionic intermediate 12, which will subsequently lead to the

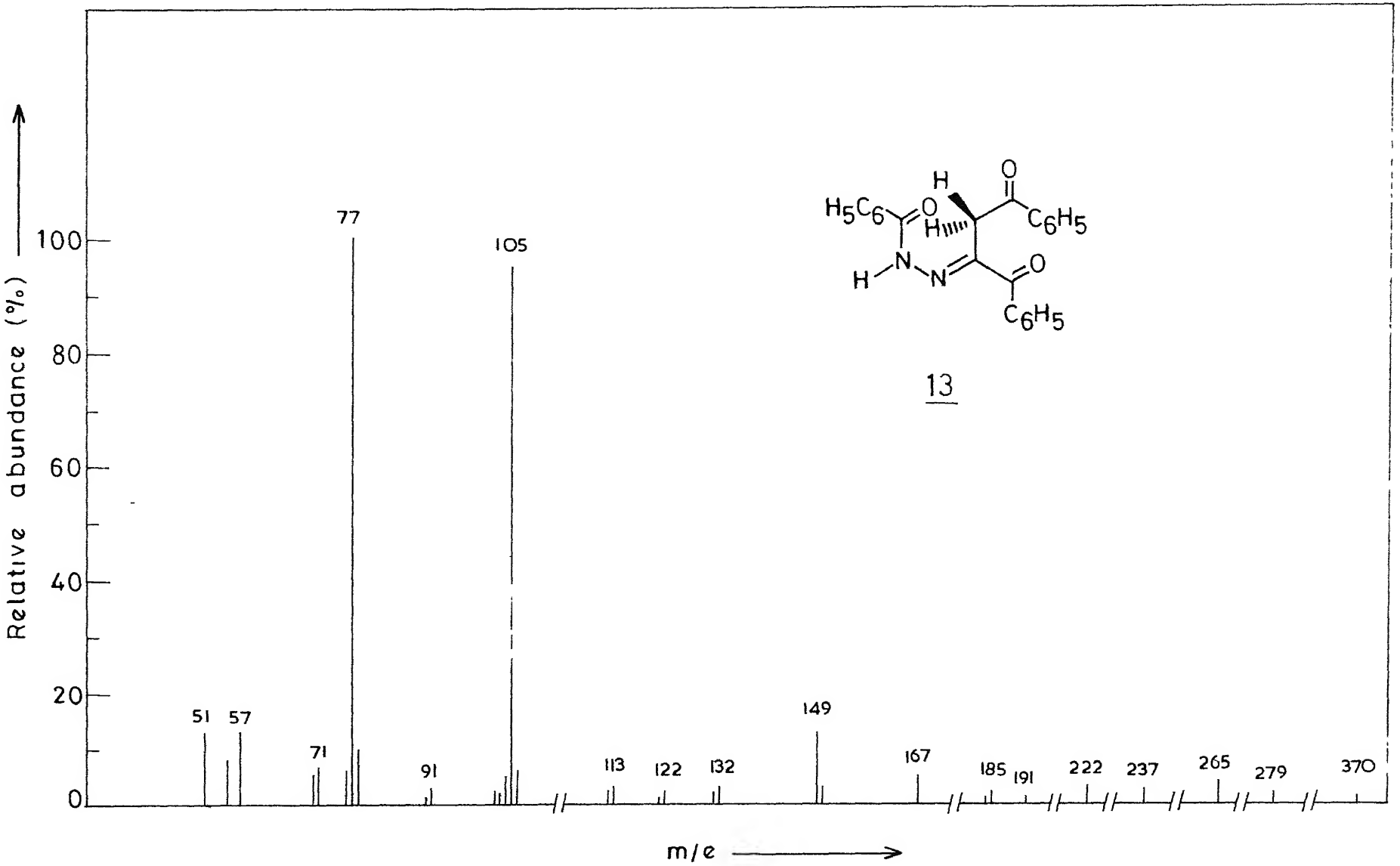
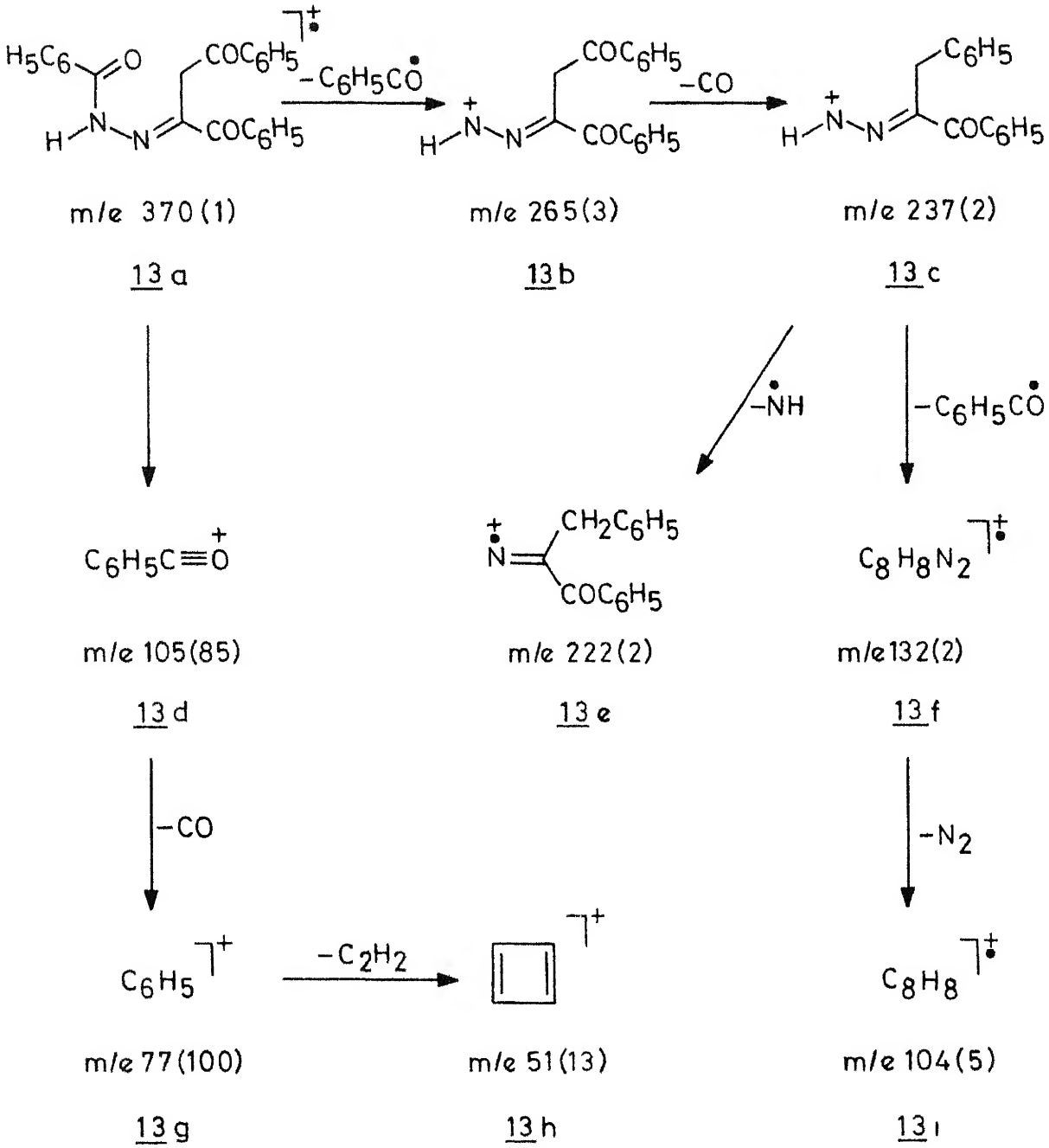


Fig. II . 2 Mass spectrum of 13 .

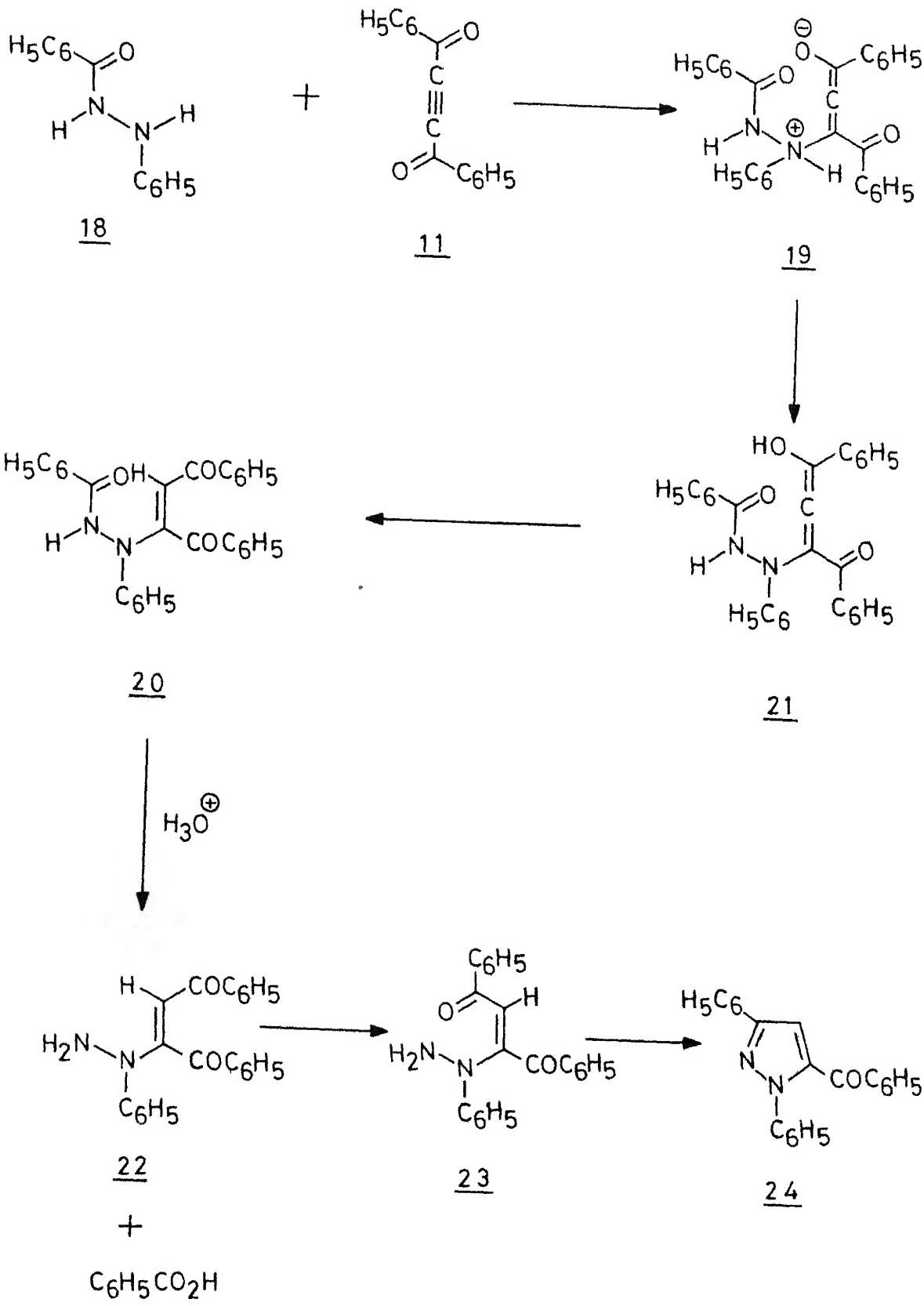
Scheme II.4


m/e 370(1)
13a
m/e 265(3)
13b
m/e 237(2)
13c
m/e 105(85)
13d
m/e 222(2)
13e
m/e 132(2)
13f
m/e 77(100)
13g
m/e 51(13)
13h
m/e 104(5)
13i

allenic alcohol 15, either through internal or external protonation. Subsequent transformation of 15, either through 14 or any of its other tautomers will lead to 13. It might be mentioned in this connection that allenic alcohol intermediates analogous to 15, have been detected spectroscopically, in the reaction of methyl mercaptan with acetylenic ketones at low temperatures ($-75^{o}C$).[10] The formation of the pyrazole 17, on treatment of 13 with either methanolic-hydrochloric acid or orthophosphoric acid can be understood in terms of the initial formation of 16, which subsequently cyclizes with the loss of elements of water, as shown in Scheme II.3

The reaction of benzoylphenylhydrazine (18) with DBA (11) in methanol at room temperature, likewise, gave a 89% yield of 2-(2'-benzoyl-1'-phenylhydrazo)-1,4-diphenylbut-2-ene-1,4-dione (20) (Scheme II.5). The IR spectrum of 20, showed an NH absorption at 3260 cm^{-1} and carbonyl absorptions at 1695 and 1670 cm^{-1}, respectively. By concentration dependent IR studies, it has been observed that 20 exhibits a weak intermolecular hydrogen-bonding in solutions. The NMR spectrum of 20 (Fig. II.3) showed a broad singlet at δ 2.90 (1 H and D_2O-exchangeable) which has been assigned to the NH proton, whereas the olefinic proton appeared as a sharp singlet at δ 6.48. The aromatic protons appeared as a complex multiplet centred around δ 7.70 (20 H).

Scheme II 5



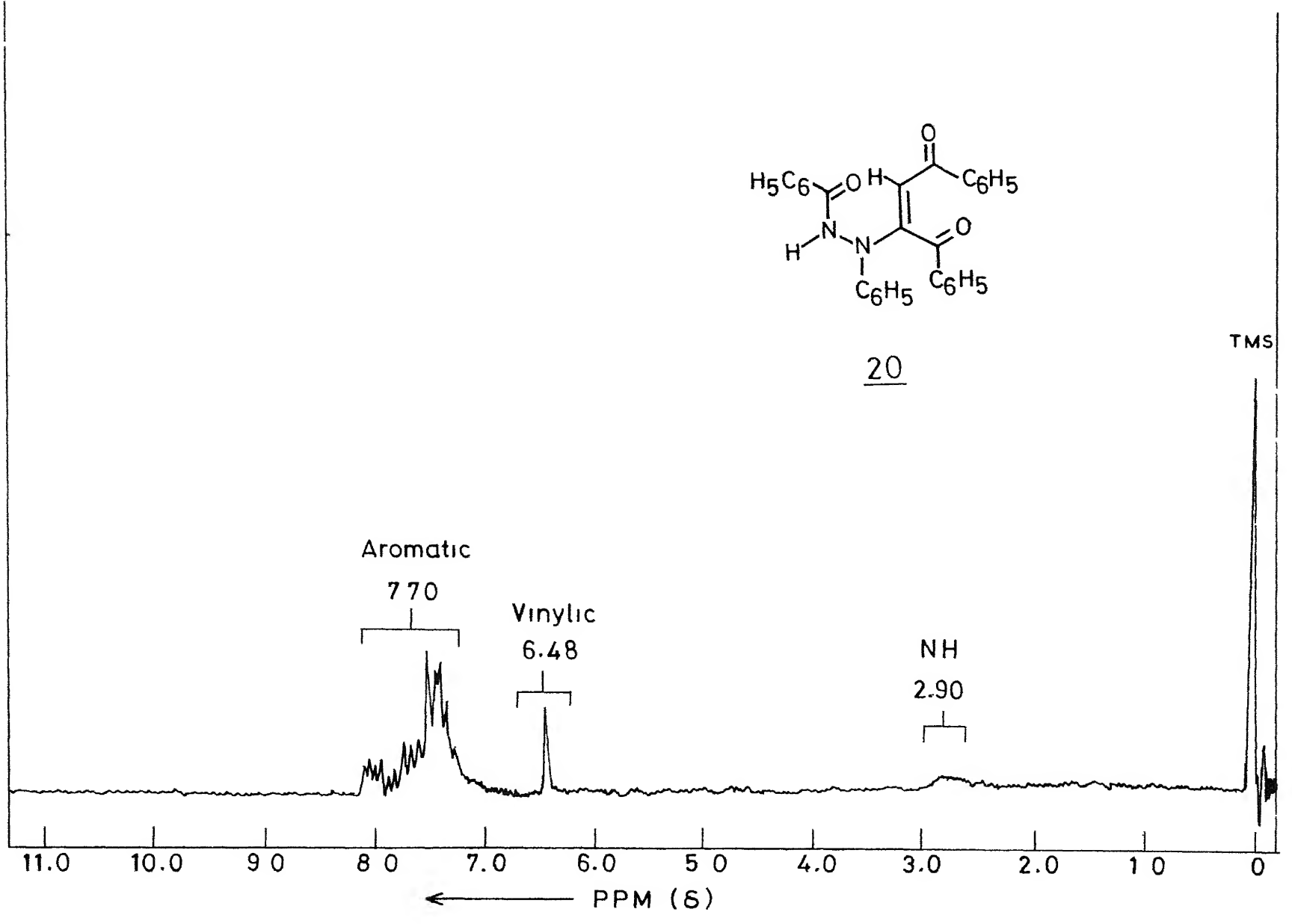


Fig. II. 3 NMR spectrum (60 MHz) of 20.

The mass spectrum of 20 (Fig. II.4) showed a molecular ion peak at m/e 446 (1). Other peaks in the spectrum were observed at m/e 341 (12), 326 (2), 325 (3), 324 (2), 323 (2), 298 (2), 222 (2), 193 (1), 167 (12), 149 (14), 105 (100), 92 (6) and 77 (80). Some of the possible modes of fragmentation, in tune with the assigned structure for 20, has been shown in Scheme II.6.

The UV spectrum of 20 showed two absorption maxima at 260 nm (ε , 20,100) and 340 (14,400), characteristic of enamine diones having the E-configuration across the carbon-carbon double bond.[11]

An attempted cyclization of 20 by treatment with ortho-phosphoric acid resulted in the formation of a 70% yield of benzoic acid and a 80% yield of 5-benzoyl-1,3-diphenylpyrazole (24). The IR spectrum of 24 showed a strong carbonyl absorption at 1650 cm^{-1}.[12] The NMR spectrum of 24 (Fig. II.5) showed a singlet at δ 7.05 (1 H), assigned to the β-pyrazolyl proton and a complex multiplet centred around δ 7.66 (15 H), assigned to the aromatic protons.

Further support for the structure of 24 has been derived from its mass spectrum (Fig. II.6), which showed a molecular ion peak at m/e 324 (100). Other peaks in the spectrum were observed at m/e 323 (27), 307 (6), 296 (10), 295 (6), 247 (32), 219 (11), 202 (3), 192 (5), 190 (3), 180 (7), 162 (11), 116 (36), 105 (61),

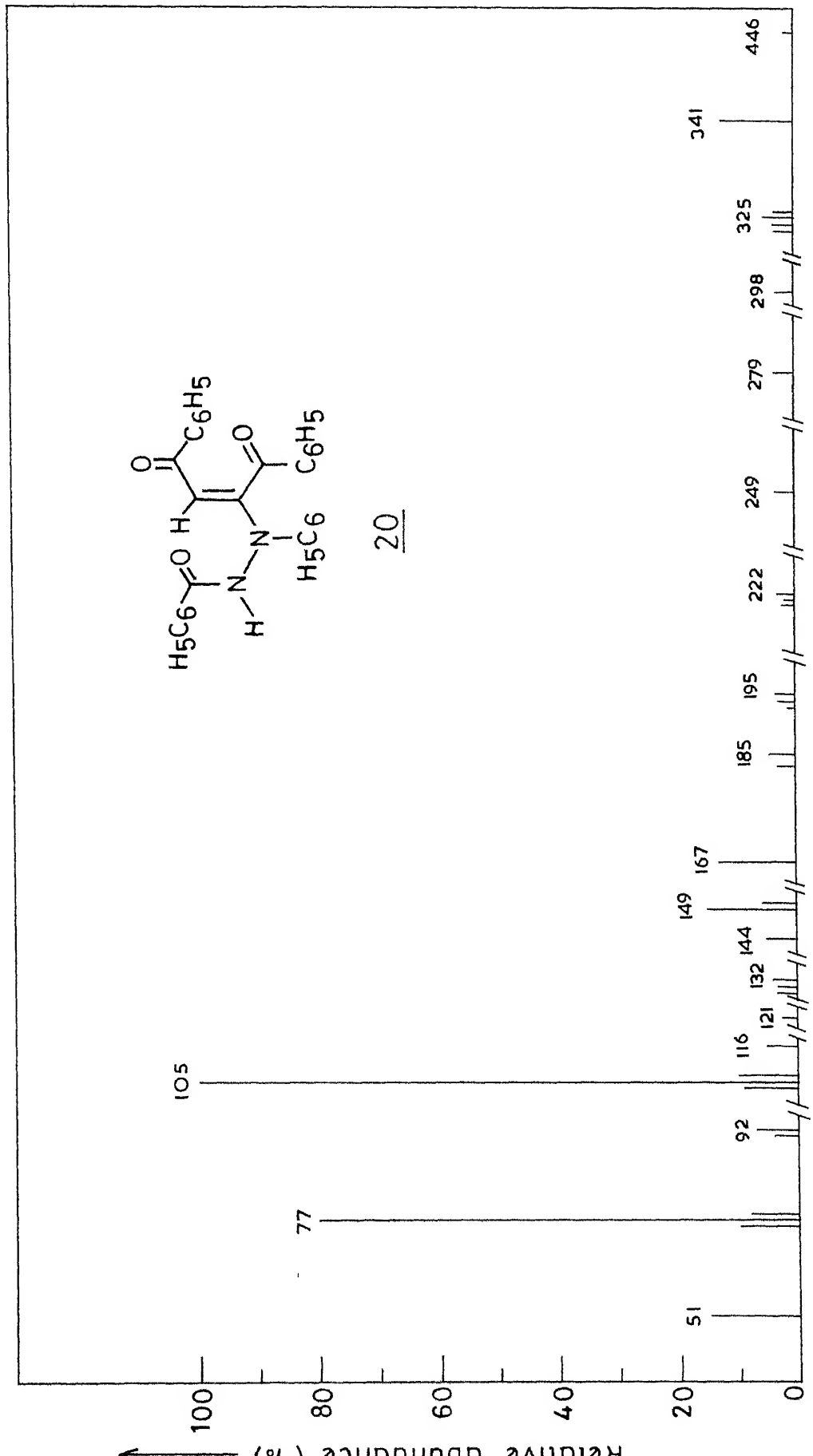
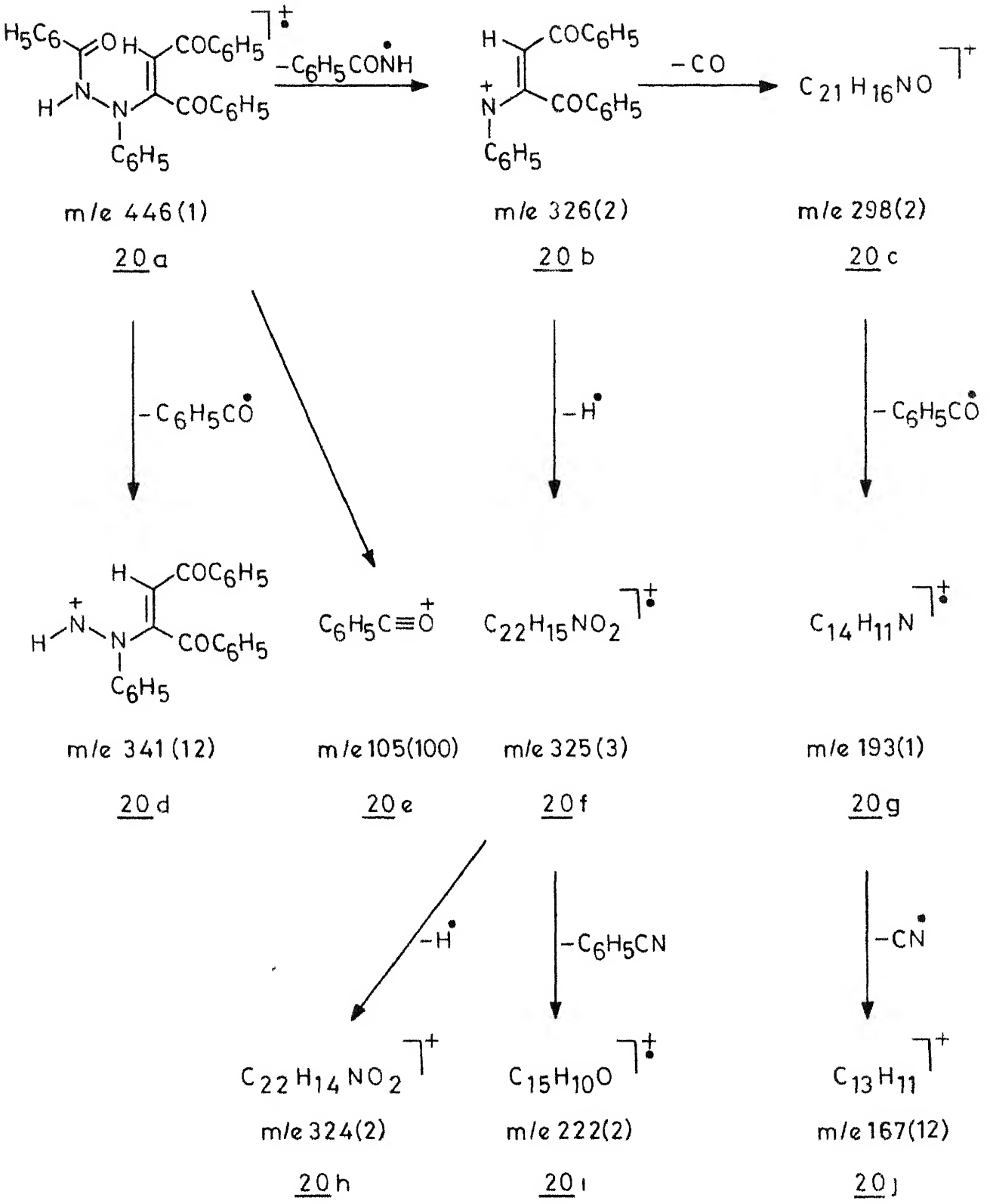
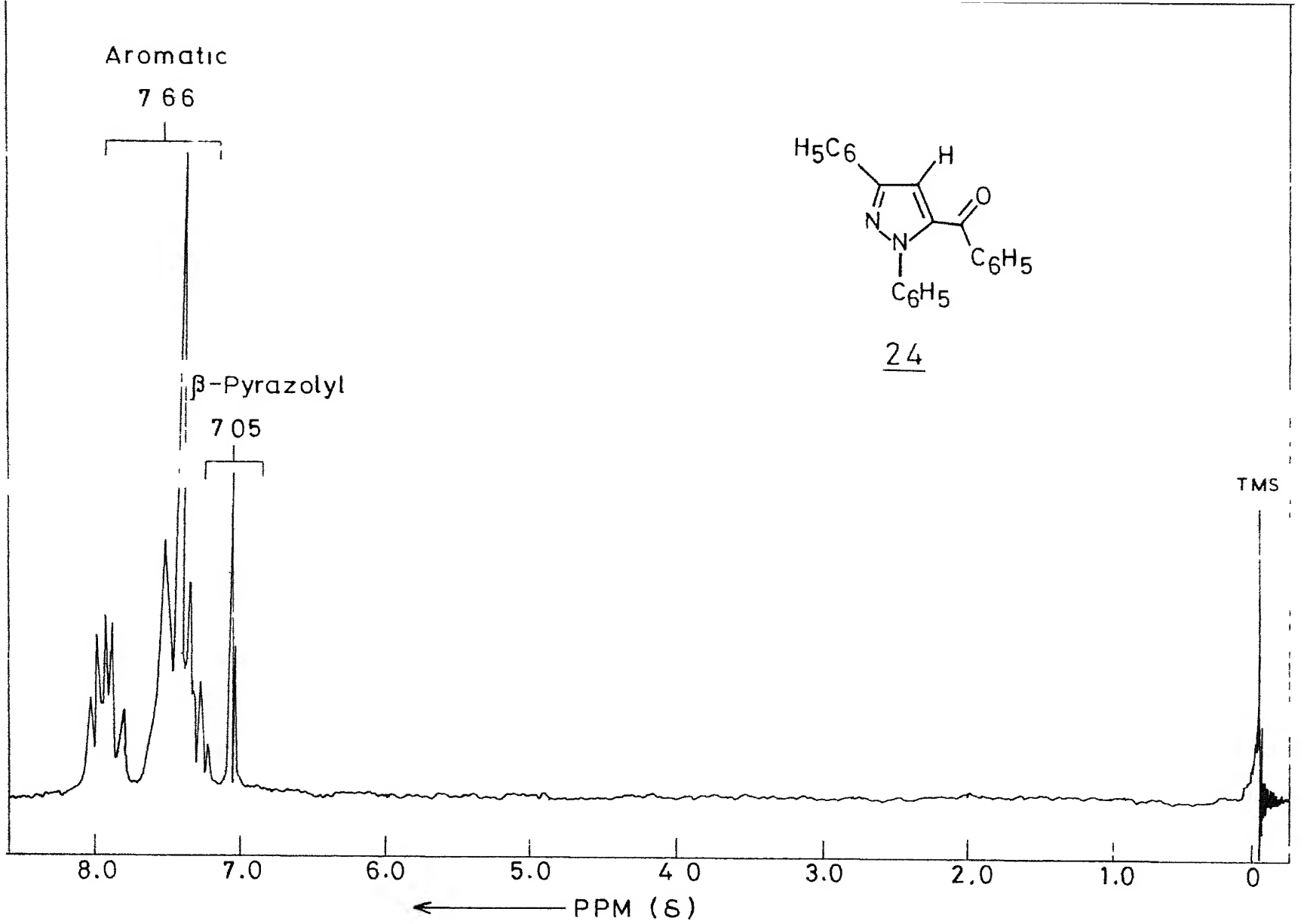


Fig. II.4 Mass spectrum of 20.

Scheme II.6


m/e 446(1)
20a
m/e 326(2)
20b
m/e 298(2)
20c
m/e 341(12)
20d
m/e 105(100)
20e
m/e 325(3)
20f
m/e 193(1)
20g
m/e 324(2)
20h
m/e 222(2)
20i
m/e 167(12)
20j



24

Fig. II 5 NMR spectrum (60 MHz) of 24.

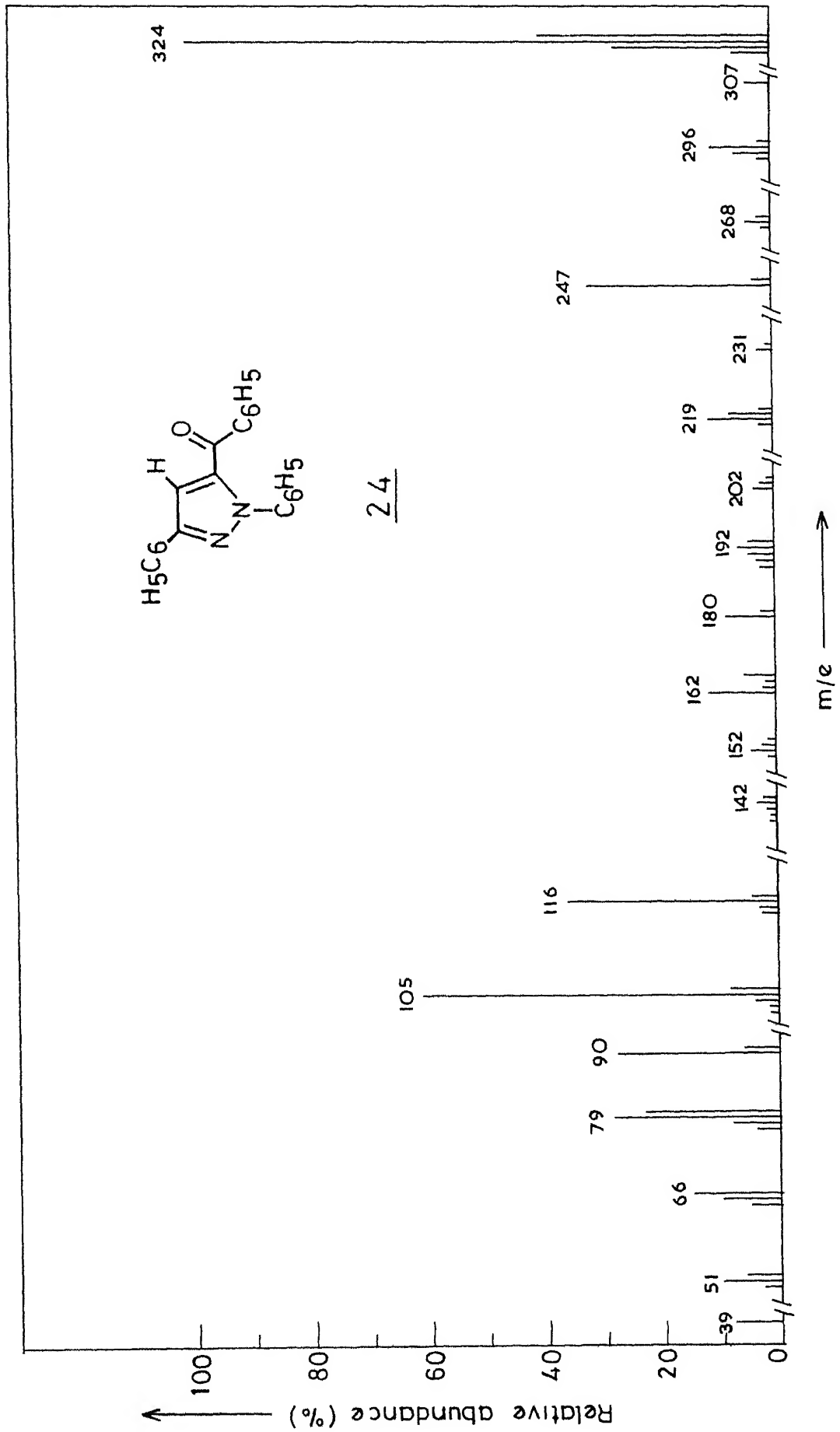


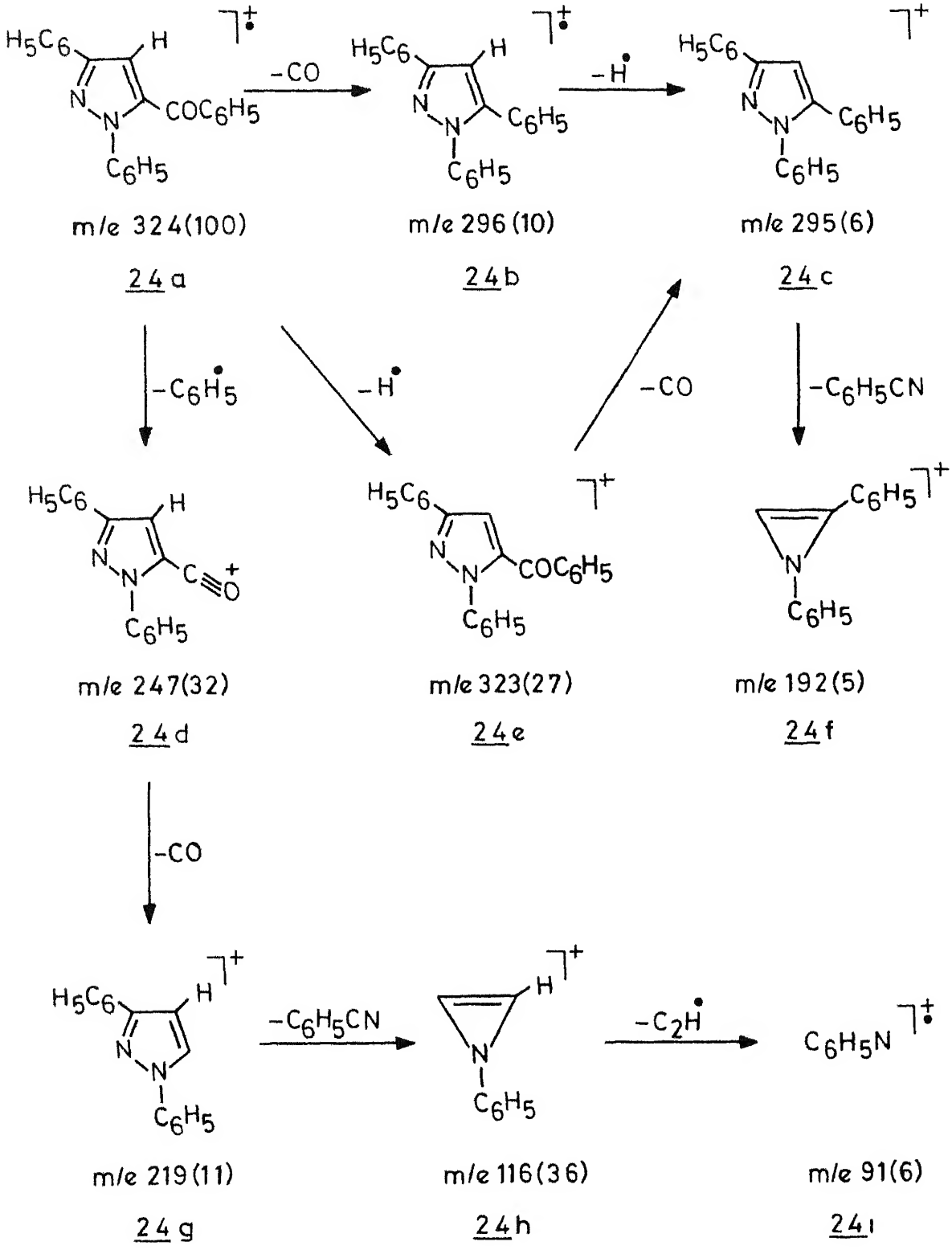
Fig. II.6 Mass spectrum of 24.

91 (6), 77 (4) and 51 (10). It may be mentioned here that the mass spectra of pyrazoles, in general, show molecular ion peaks as base peaks. In addition, the presence of prominent (M^+-1) peaks have been observed in the mass spectra of pyrazole derivatives.[13] Both these features have been observed in the spectrum of 24. Some of the probable modes of fragmentation of 24, under electron impact, are shown in Scheme II.7.

A probable route to the formation of 20 in the reaction of 18 with DBA and the subsequent transformation of 20, under acid-catalysed conditions, to 24 are shown in Scheme II.5. It is assumed that the initially formed zwitterionic intermediate 19, undergoes either internal or external protonation to give the allenic alcohol 21, which will then be converted to 20 The fact that the formation of 20 is not observed when the reaction of 18 with DBA is carried out in an aprotic solvent such as THF would probably suggest that the zwitterionic intermediate 19, does not undergo internal protonation efficiently.

The formation of the pyrazole 24, on treatment of 20 with orthophosphoric acid may be rationalized in terms of the initial formation of the enehydrazine dione 22, of E-configuration, which subsequently undergoes isomerisation to the Z-isomer, 23, followed by the cyclization of 23, with the loss of elements of water. It may be pointed out here that several examples of the E-Z isomerisation of enamine diones under acid-catalysed

Scheme II.7


-CO
-H
-C6H5
-H
-CO
-C6H5CN
-CO
-C6H5CN
-C2H
m/e 324(100)
24a
m/e 296(10)
24b
m/e 295(6)
24c
m/e 247(32)
24d
m/e 323(27)
24e
m/e 192(5)
24f
m/e 219(11)
24g
m/e 116(36)
24h
m/e 91(6)
24i

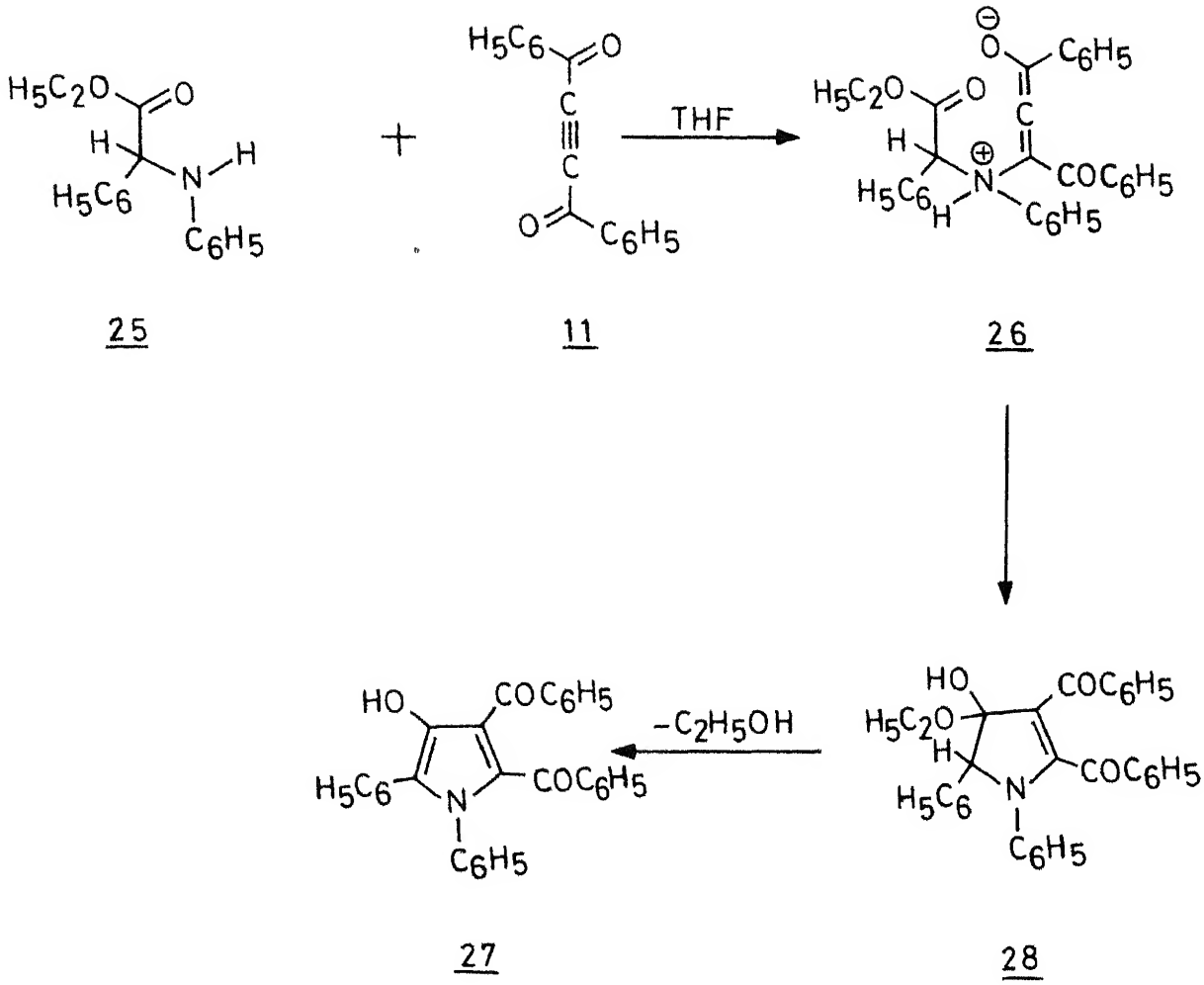
conditions are reported in the literature.[14]

In continuation of our studies, we have examined the reaction of an α-amino acid ester such as ethyl N,C-diphenylglycinate (25) with DBA. Treatment of equimolar amounts of 25 and DBA in THF at room temperature resulted in the formation of a 90% yield of 2,3-dibenzoyl-4-hydroxy-1,5-diphenylpyrrole (27) (Scheme II.8). The IR spectrum of 27 showed a hydroxyl absorption at 3320 cm^{-1} and two carbonyl absorptions at 1640 and 1620 cm^{-1}, respectively The NMR spectrum of 27 (Fig. II.7) showed a sharp singlet at δ 8.85 (1 H, exchangeable with D_2O), which has been assigned to the hydroxyl proton and a multiplet centred around δ 7.22 (20 H) which has been assigned to the aromatic protons.

The formation of the pyrrole 27 in the reaction of ethyl N,C-diphenylglycinate (25) and DBA can be understood in terms of the pathway shown in Scheme II.8. It has been assumed that the zwitterionic intermediate 26 is formed initially, which undergoes cyclization to give the pyrroline derivative 28, which in turn loses elements of ethanol to give 27.

In continuation, we have examined the reactions of a few aldehyde and ketone hydrazones and phenylhydrazones with DBA, with a view to studying the nature of the products formed in these cases. The hydrazones and phenylhydrazones that we have examined include benzaldehyde hydrazone (29a), benzophenone

Scheme II.8



25 11 26

28 27

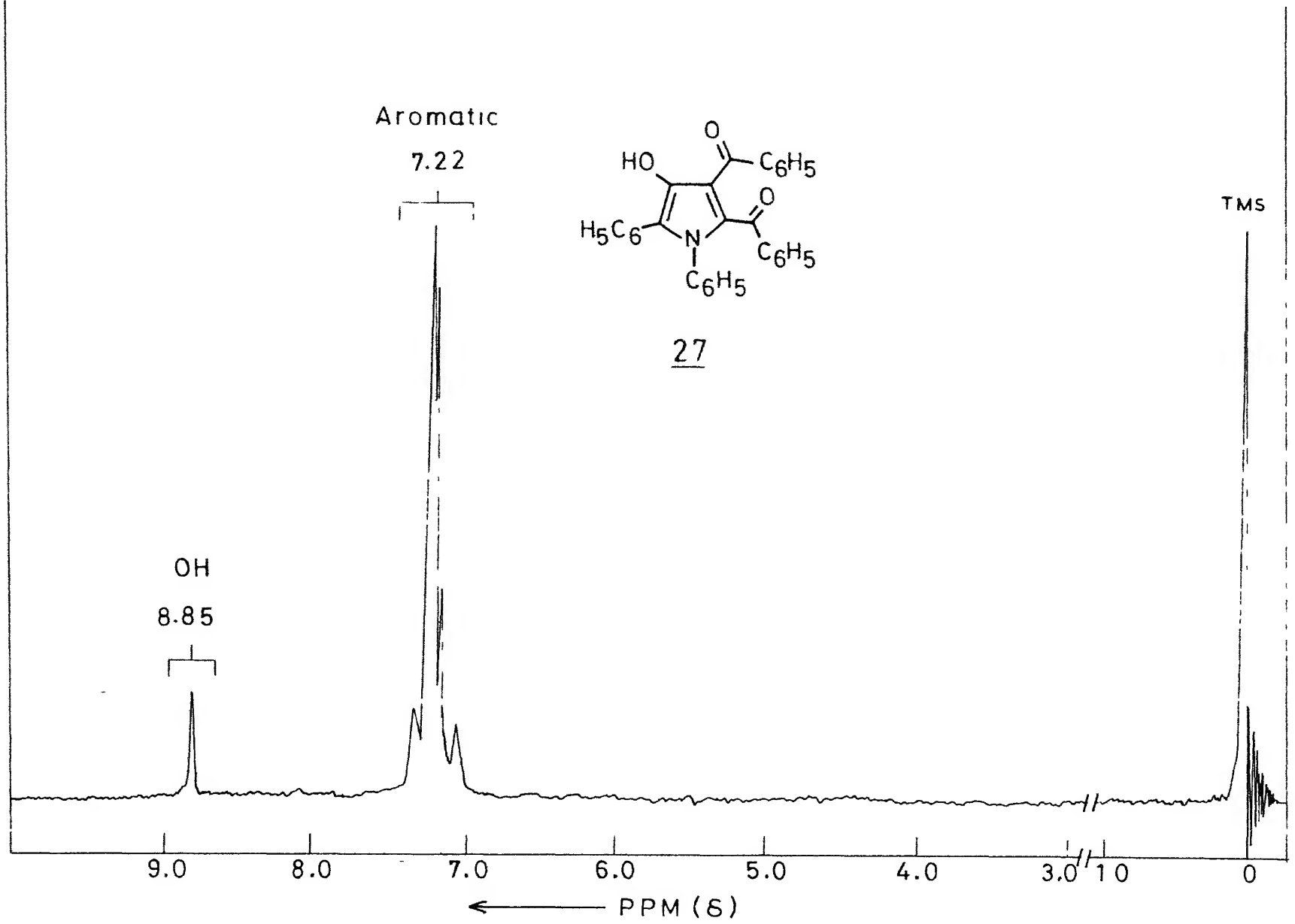


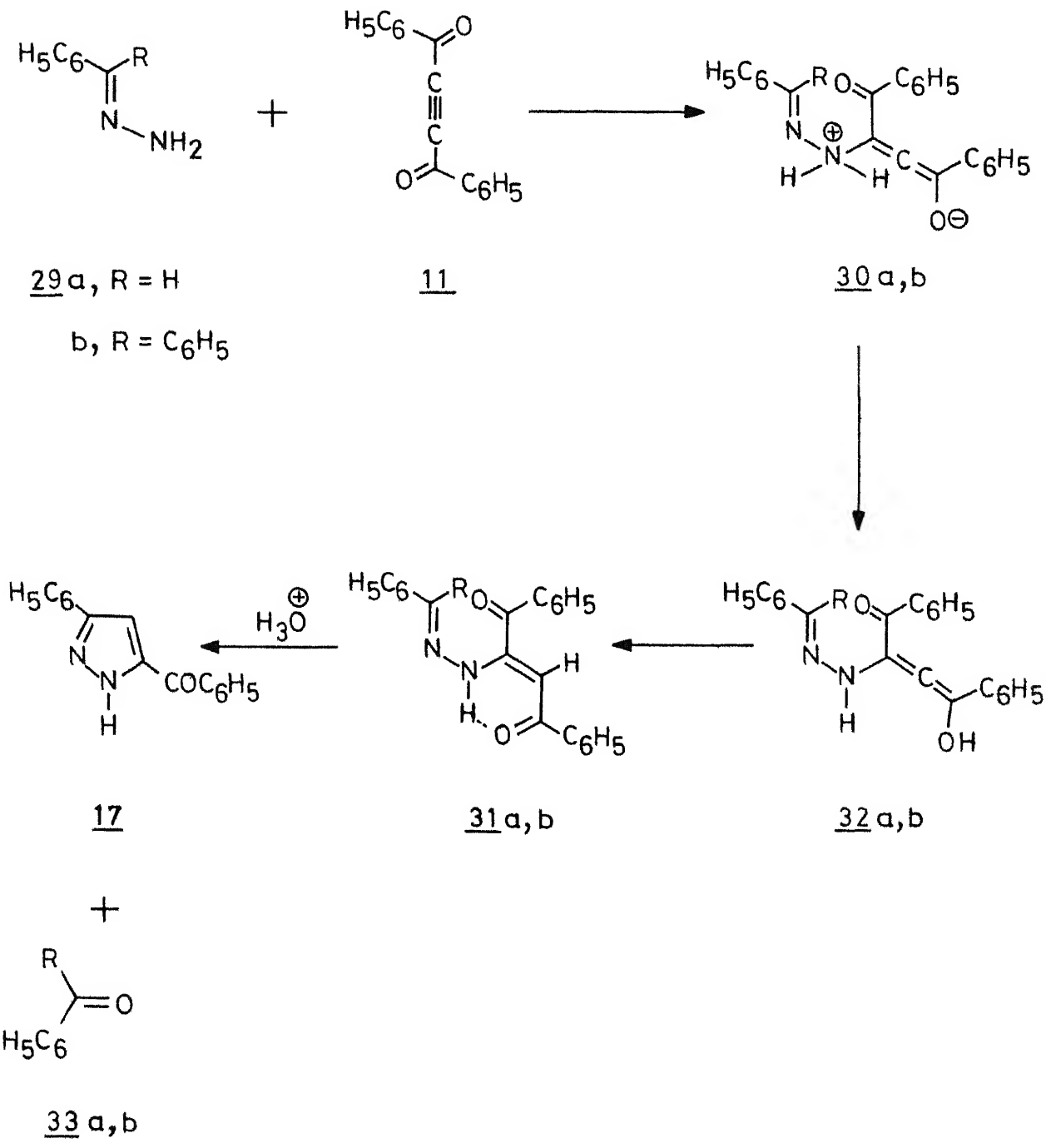
Fig. II.7 NMR spectrum (60 MHz) of 27.

hydrazone (29b), benzaldehyde phenylhydrazone (34a) and p-anisaldehyde phenylhydrazone (34b). Treatment of an equimolar mixture of 29a and DBA in methanol at room temperature, for example, gave a 88% yield of 2-(1'-hydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (31a). Similarly, the reaction of benzophenone hydrazone (29b) with DBA in methanol gave a 93% yield of 2-(1'-hydrazinyl-2'-benzhydrylidene)-1,4-diphenylbut-2-ene-1,4-dione (31b) (Scheme II.9).

The structures of both 31a and 31b have been arrived at on the basis of analytical data, spectral evidences and chemical transformations. The IR spectrum of 31a, for example, showed an intramolecularly hydrogen-bonded NH band at 3090 cm^{-1} and a carbonyl absorption band at 1675 cm^{-1}. The NMR spectrum of 31a (Fig. II.8) showed a singlet at δ 6.00 (1 H), assigned to the vinylic proton and a complex multiplet centred around δ 7.72 (16 H), assigned to the aromatic and benzylidene protons. In addition, the spectrum showed a singlet at δ 13.38 (1 H, D_2O-exchangeable), assigned to the NH proton.

The mass spectrum of 31a (Fig. II.9) showed a molecular ion peak at m/e 354 (17). Other peaks in the spectrum were observed at 336 (2), 326 (1), 308 (1), 250 (24), 249 (100), 248 (3), 220 (18), 181 (8), 171 (16), 146 (34), 105 (32), 104 (32), 103 (32), 77 (32) and 51 (32). Some of the probable fragmentation modes are shown in Scheme II.10.

Scheme II 9



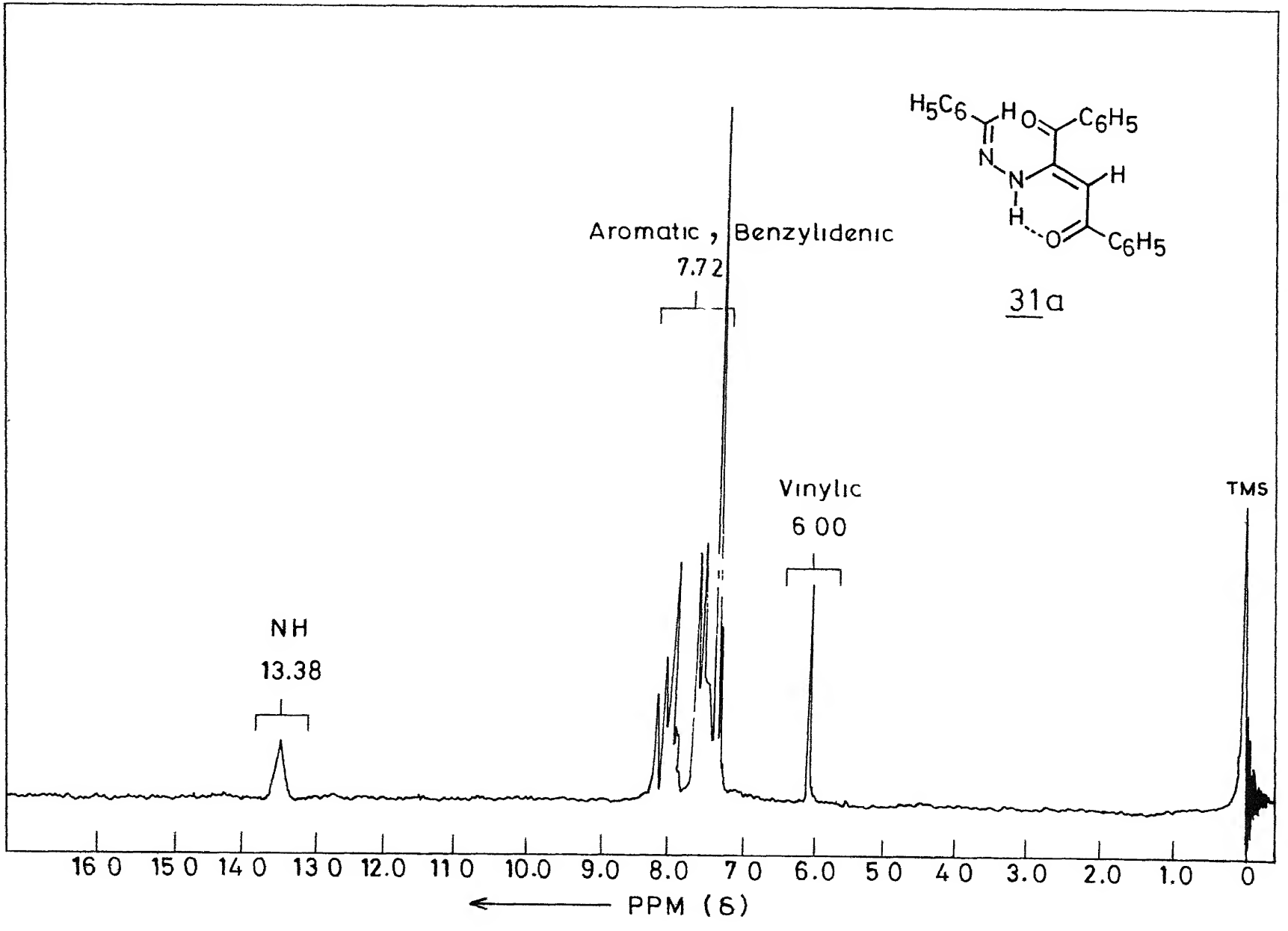


Fig II.8 NMR spectrum (60 MHz) of 31a.

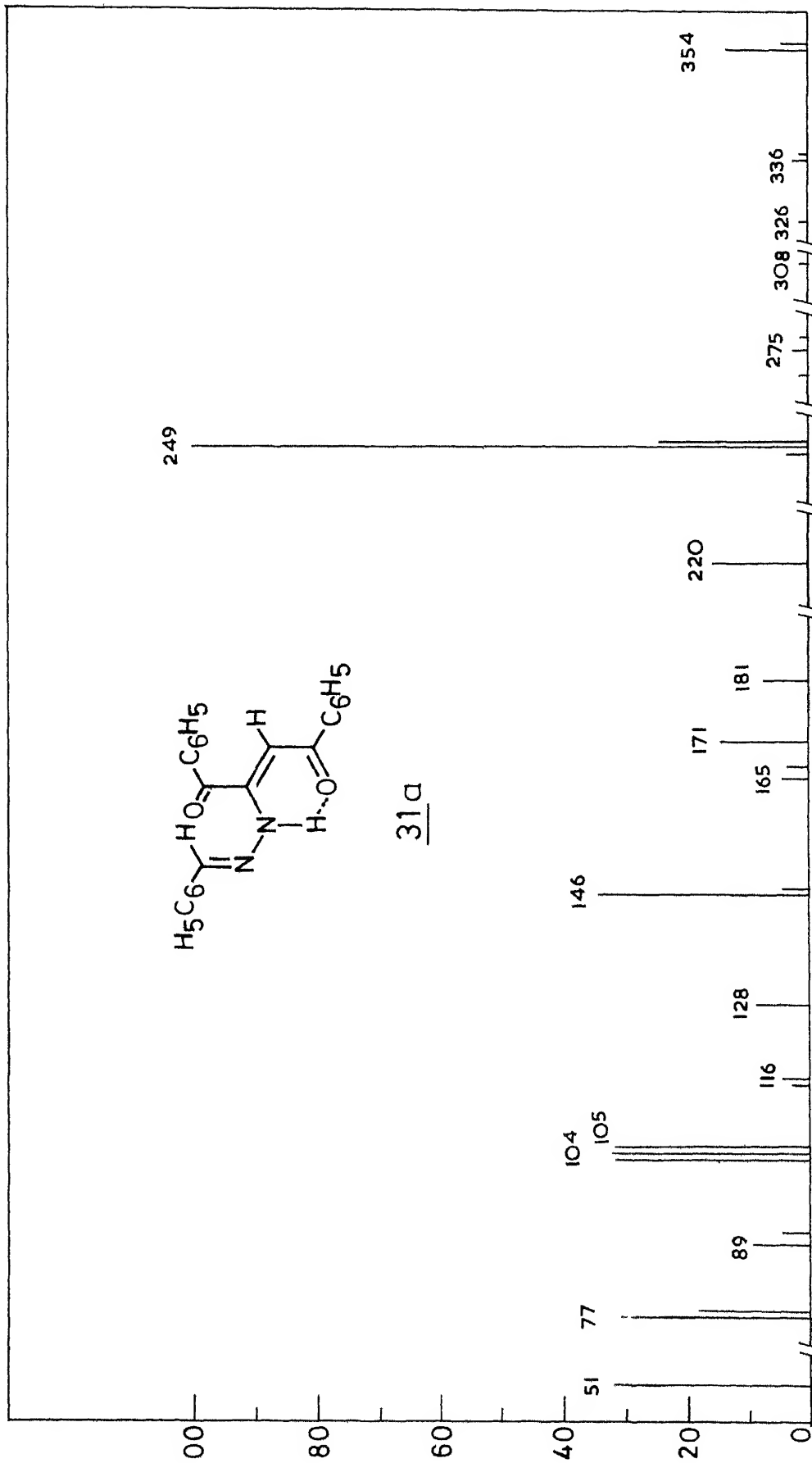
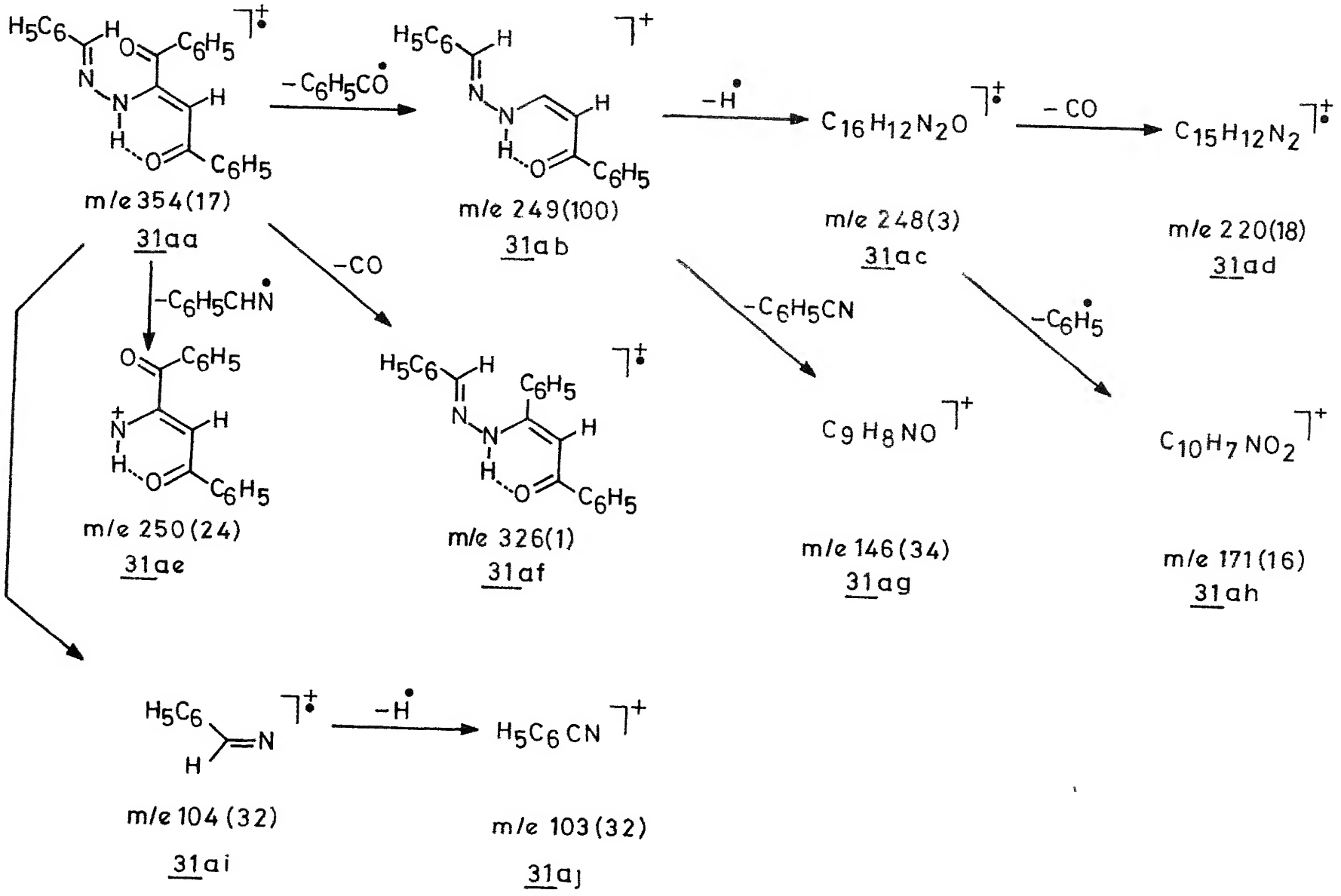


Fig. II.9 Mass spectrum of 31a.

Scheme II 10


m/e 354(17)
31aa
-C6H5CO
m/e 249(100)
31ab
-H
C16H12N2O
m/e 248(3)
31ac
-CO
C15H12N2
m/e 220(18)
31ad
-C6H5CHN
m/e 250(24)
31ae
-CO
m/e 326(1)
31af
-C6H5CN
C9H8NO
m/e 146(34)
31ag
-C6H5
C10H7NO2
m/e 171(16)
31ah
m/e 104(32)
31ai
-H
H5C6CN
m/e 103(32)
31aj

Similarly, the IR spectrum of 31b showed an intramolecularly hydrogen-bonded NH absorption around 3160-2980 cm^{-1} and a carbonyl absorption band at 1675 cm^{-1}. The NMR spectrum of 31b (Fig. II.10) showed a singlet at δ 5.95 (1 H), assigned to the vinylic proton, whereas the aromatic protons appeared as a complex multiplet centred around δ 7.71 (20 H). In addition, the spectrum showed a singlet at δ 12.78 (1 H), which was exchangeable with D_2O and was assigned to the NH proton.

The mass spectrum of 31b (Fig. II.11) showed a molecular ion peak at m/e 430 (7). Other peaks in the spectrum were observed at m/e 412 (2), 386 (1), 353 (1), 325 (37), 297 (1), 250 (3), 220 (1), 180 (100), 166 (10), 154 (2), 105 (35), 77 (20) and 51 (20). Some of the probable fragmentation modes of 31b are shown in Scheme II.11.

Additional evidence for the structures of both 31a and 31b is derived from the fact that they gave the same pyrazole, namely, 5-benzoyl-3-phenylpyrazole (17), on treatment with methanolic hydrochloric acid (Scheme II.9).

The formation of the products such as 31a and 31b in the reactions of benzaldehyde hydrazone (29a) and benzophenone hydrazone (29b), respectively with DBA can be rationalized in terms of the pathways shown in Scheme II.9.

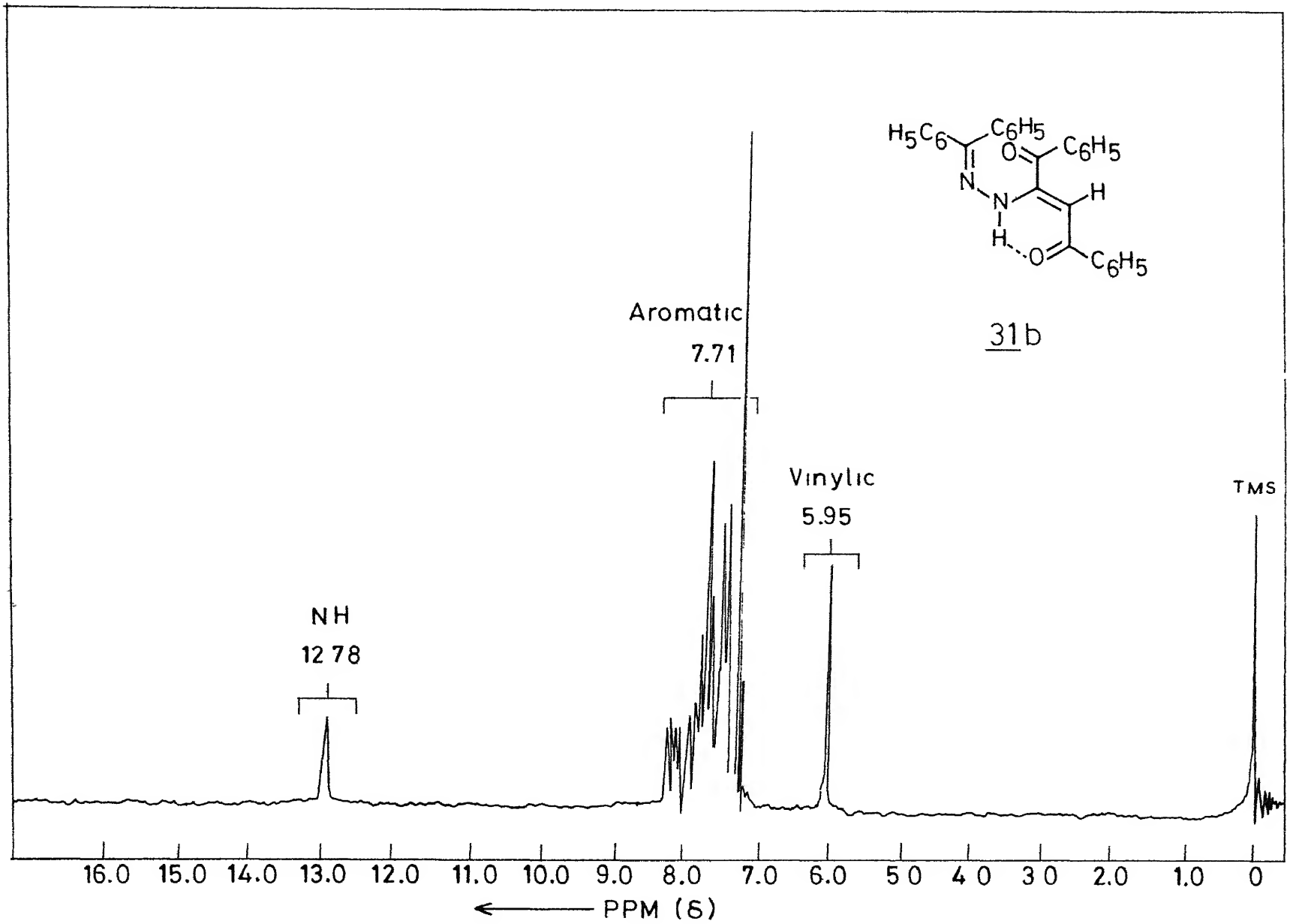


Fig. II. 10 NMR spectrum (60 MHz) of 31b.

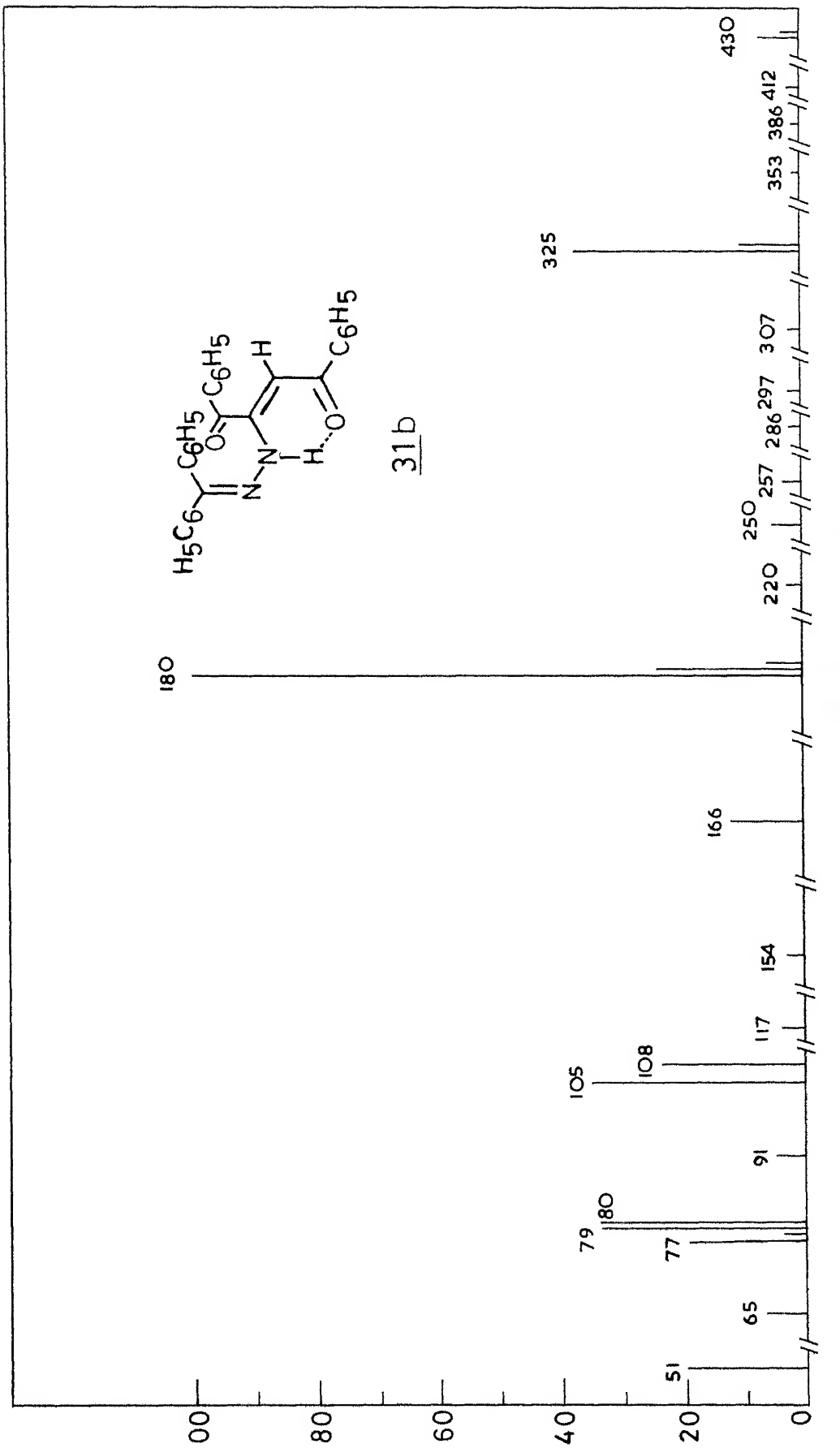
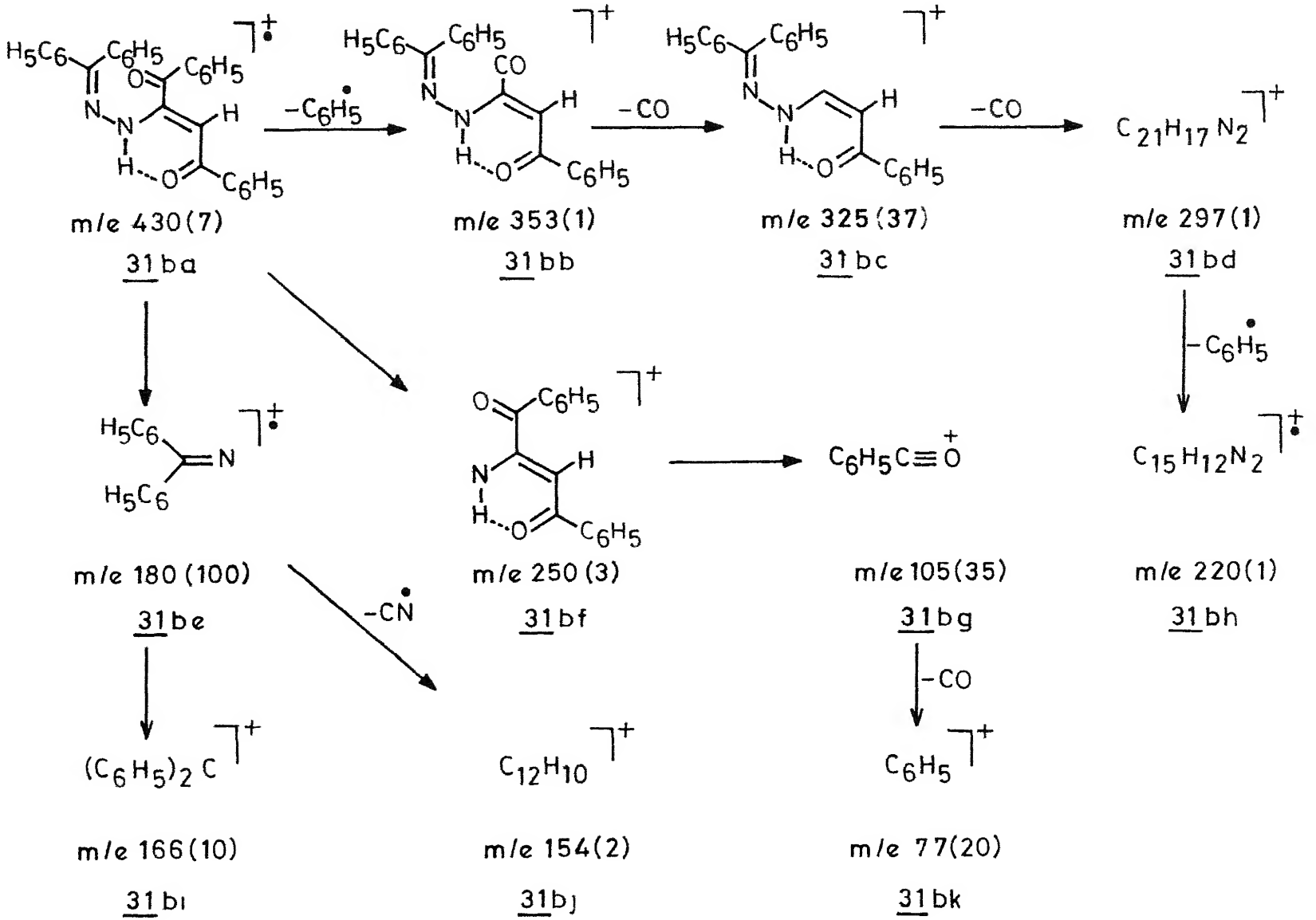


Fig. II.11 Mass spectrum of 31b

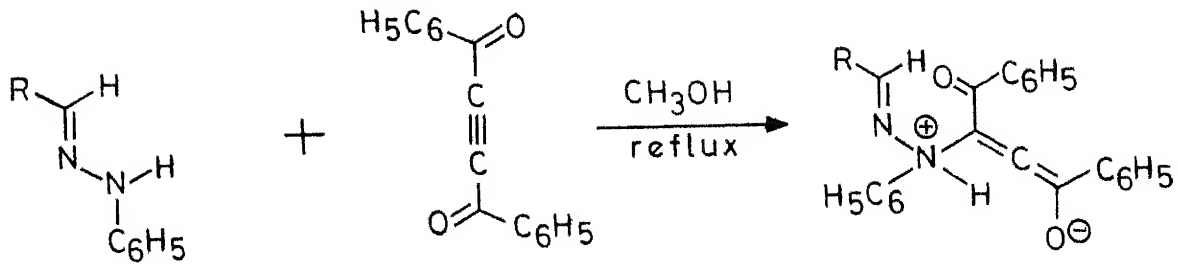
Scheme II.11


m/e 430(7)
31ba
-C6H5
m/e 353(1)
31bb
-CO
m/e 325(37)
31bc
-CO
C21H17N2
m/e 297(1)
31bd
-C6H5
C15H12N2
m/e 220(1)
31bh
m/e 180(100)
31be
-CN
m/e 250(3)
31bf
C6H5C≡O
m/e 105(35)
31bg
-CO
(C6H5)2C
m/e 166(10)
31bi
C12H10
m/e 154(2)
31bj
C6H5
m/e 77(20)
31bk

The reaction of benzaldehyde phenylhydrazone (34a) with DBA in refluxing methanol, on the other hand, gave a mixture of products consisting of 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (38, 8%), 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenyl-but-2-ene-1,4-dione (39a, 19%) and an unidentified product, 36, mp 250-251° (d). Similarly, the reaction of p-anisaldehyde phenylhydrazone (34b) with DBA in refluxing methanol gave a mixture of products consisting of 38 (8%), 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (39b, 15%) and a small quantity of an unidentified product, 37, mp 238° (d) (Scheme II.12). The structures of both 39a and 39b have been assigned on the basis of analytical data and spectral evidences.

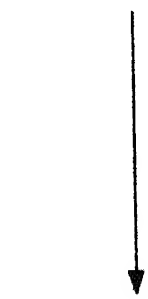
The IR spectrum of 39a, for example, showed a carbonyl absorption at 1685 cm^{-1}. The NMR spectrum of 39a (Fig. II.12) showed a sharp singlet at δ 6.00 (1 H), assigned to the vinylic proton and a complex multiplet centred around δ 7.70 (21 H), due to the aromatic and benzylidene protons. The mass spectrum of 39a (Fig. II.13) showed a molecular ion peak at m/e 430 (6). Other peaks in the spectrum were observed at m/e 326 (10), 325 (30), 279 (12), 222 (60), 221 (30), 220 (15), 219 (6), 204 (2), 185 (24), 183 (24), 167 (45), 149 (43), 119 (20), 105 (90), 77 (100) and 51 (84). Some of the probable modes of fragmentation are shown in Scheme II.13.

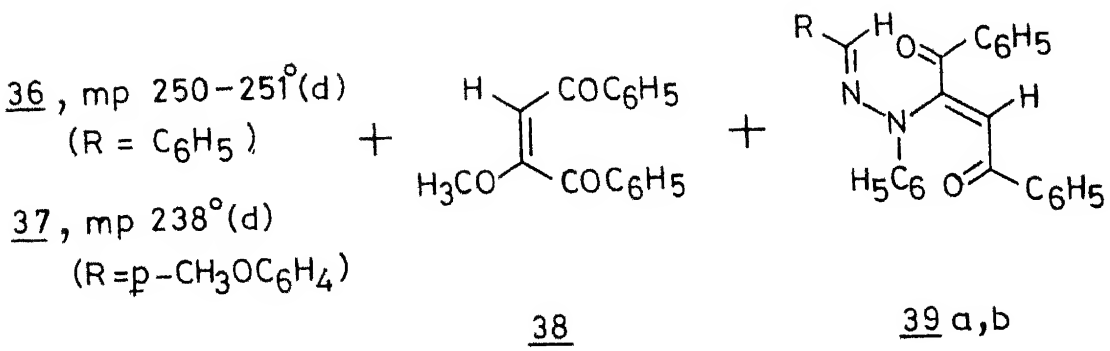
Scheme II 12



34a, R = C_6H_5 11 35a,b

b, R = p-$CH_3OC_6H_4$





36, mp 250-251°(d) (R = C_6H_5)

37, mp 238°(d) (R = p-$CH_3OC_6H_4$)

38 39a,b

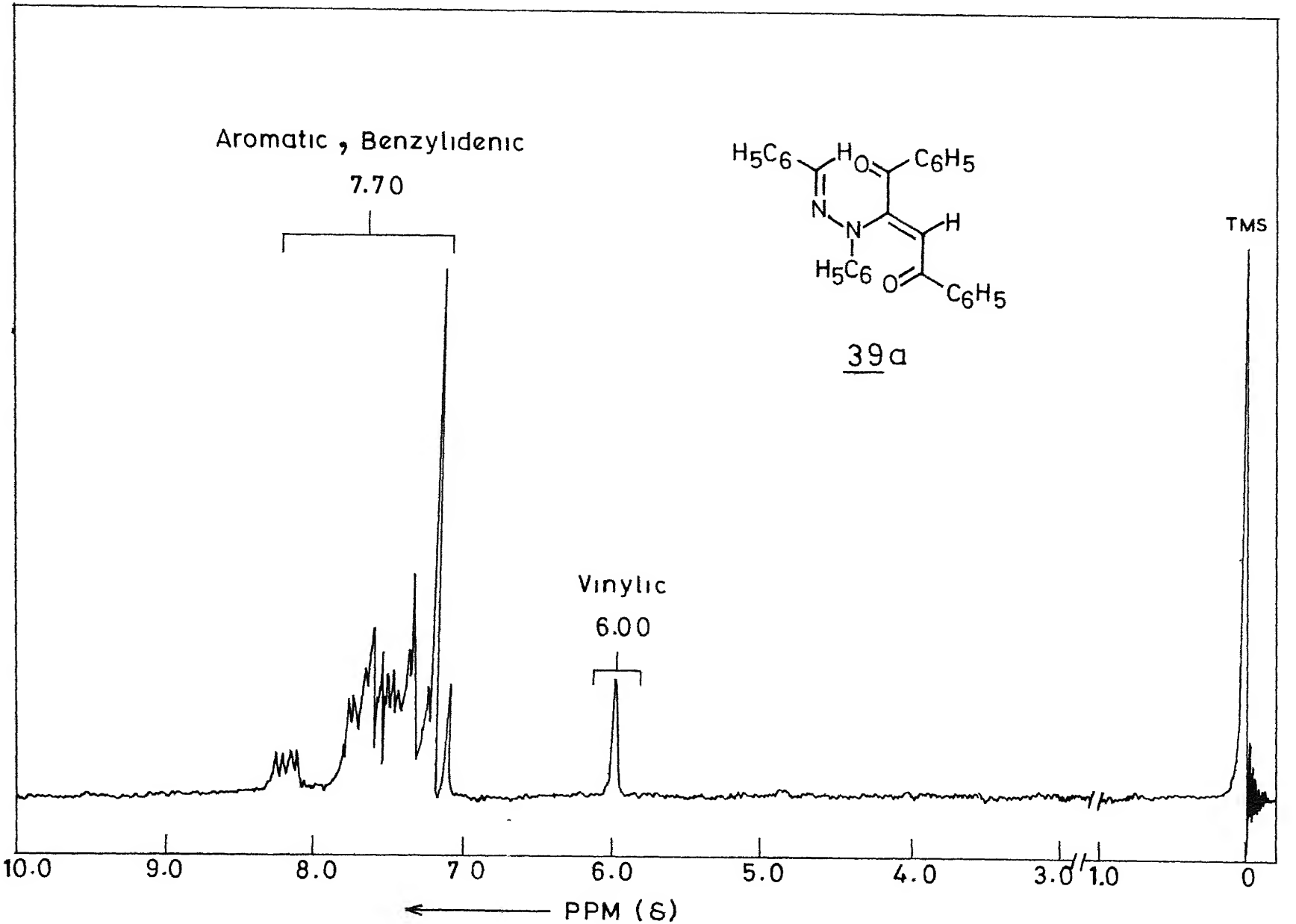


Fig. II.12 NMR spectrum (60 MHz) of 39a.

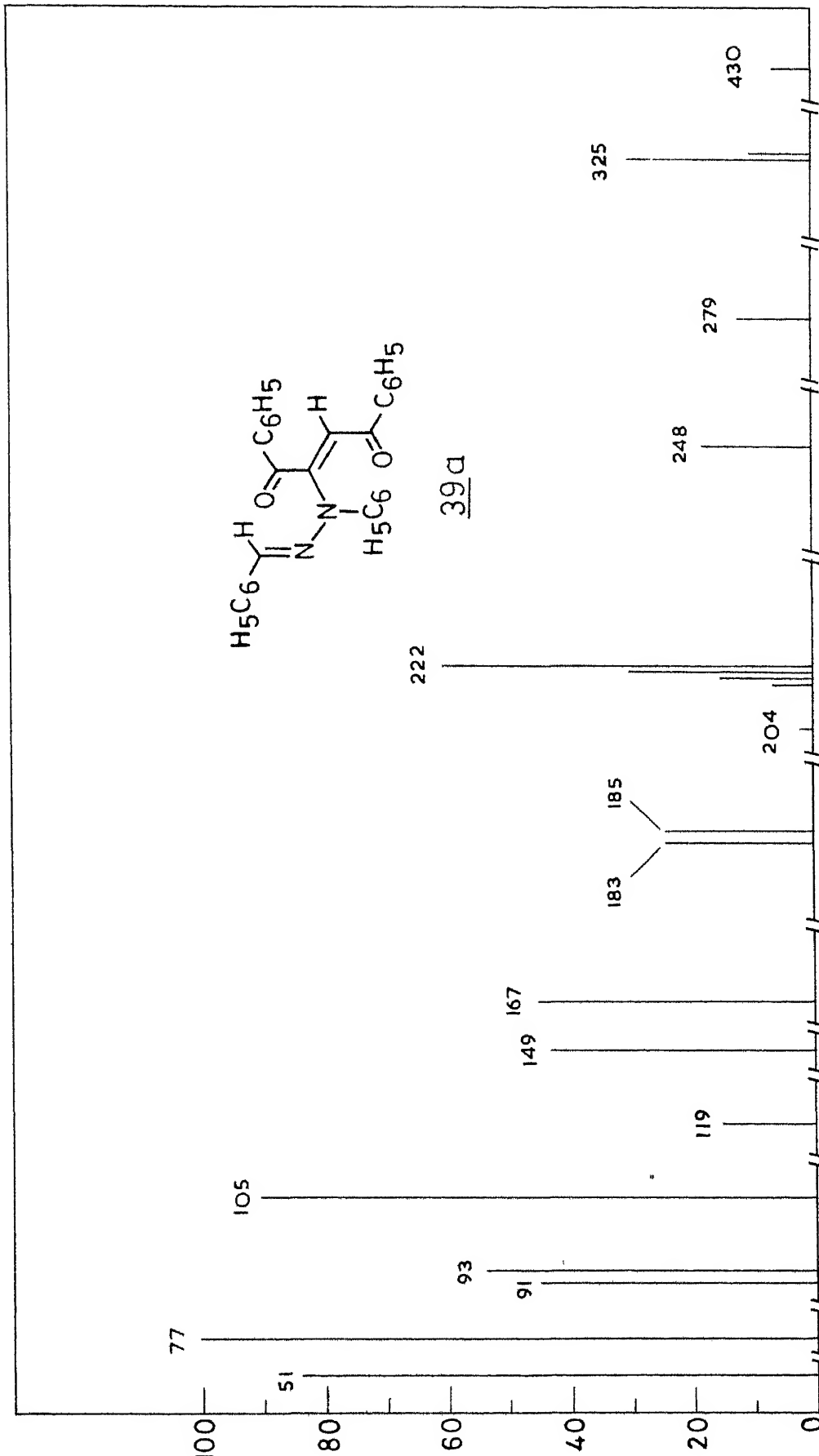
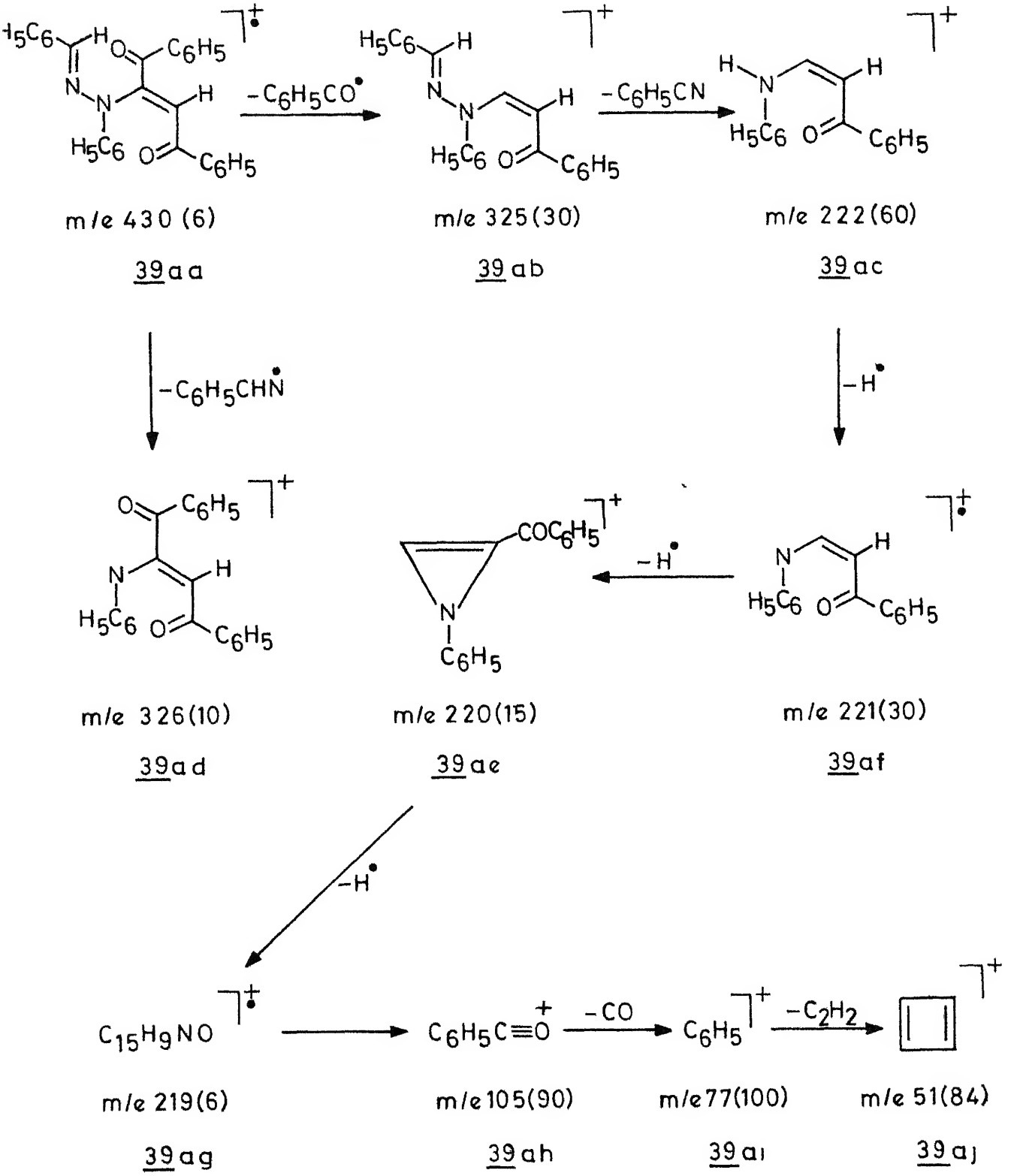


Fig. II . 13 Mass spectrum of 39a.

Scheme II.13


m/e 430 (6)
39aa
m/e 325(30)
39ab
m/e 222(60)
39ac
m/e 326(10)
39ad
m/e 220(15)
39ae
m/e 221(30)
39af
m/e 219(6)
39ag
m/e 105(90)
39ah
m/e 77(100)
39ai
m/e 51(84)
39aj

Likewise, the IR spectrum of 39b showed two carbonyl absorptions at 1685 and 1660 cm^{-1}, respectively. The NMR spectrum of 39b (Fig. II.14) showed a singlet at δ 3.72 (3 H), assigned to the methoxy protons, a second singlet at δ 5.95 (1 H), assigned to the vinylic proton and a complex multiplet centred around δ 7.21 (20 H), assigned to the aromatic and benzylidene protons. The mass spectrum of 39b (Fig II.15) showed a molecular ion peak at m/e 460 (39). Other peaks were observed at 458 (91), 450 (90), 445 (26), 429 (14), 401 (7), 381 (60), 353 (100), 327 (15), 276 (6), 222 (45), 221 (15), 193 (10), 144 (45), 134 (45), 105 (45), 77 (40), 69 (22) and 51 (10). Some of the probable fragmentation patterns are shown in Scheme II.14.

The formation of products such as 38, 39a and 39b in the reactions of 34a and 34b with DBA can be understood in terms of the pathways shown in Scheme II.12.

Further, we have examined the reactions of both benzil monohydrazone (40a) and benzil monophenylhydrazone (40b) with DBA. Treatment of equimolar amounts of 40a and DBA in refluxing xylene, for example, gave a 91% yield of 3,4-dibenzoyl-5,6-diphenylpyridazine (45) (Scheme II.15). The IR spectrum of 45 showed a carbonyl absorption at 1665 cm^{-1}. The NMR spectrum of 45 (Fig. II.16) showed a complex multiplet centred around δ 7.54 due to aromatic protons. The mass spectrum of 45 (Fig. II.17) showed a molecular ion peak at m/e 440 (100). Other peaks in

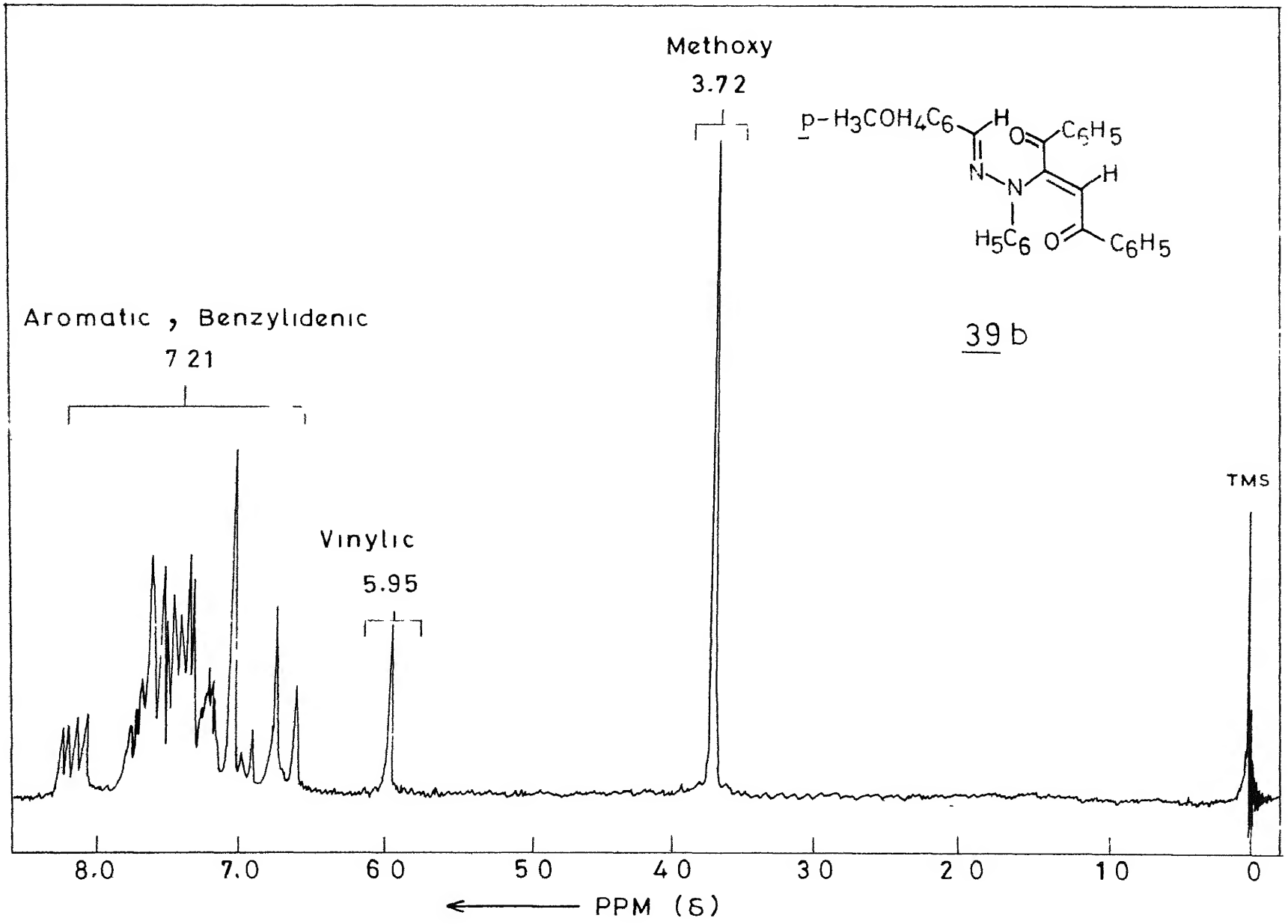


Fig. II . 14 NMR spectrum (60 MHz) of 39 b

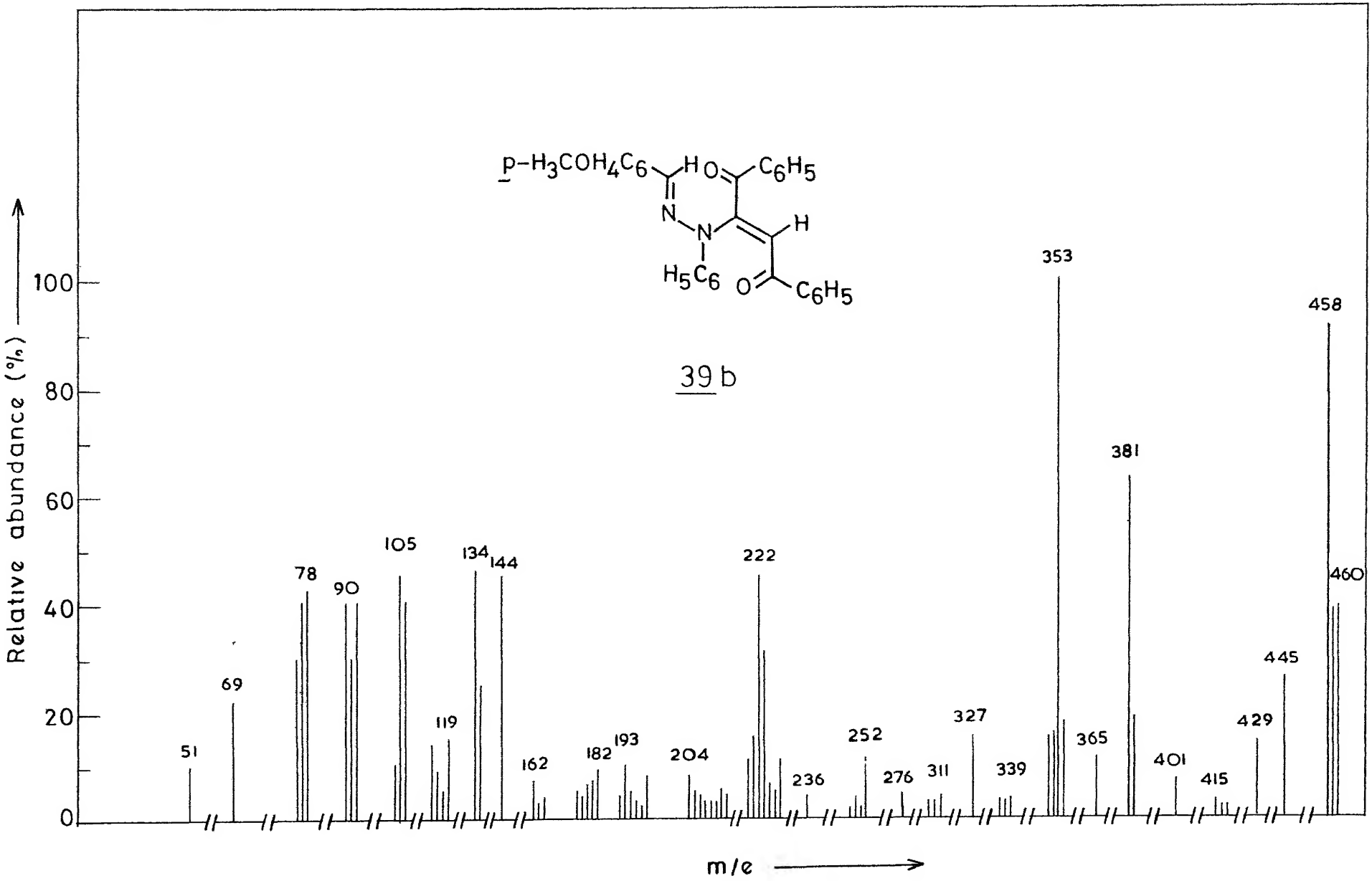
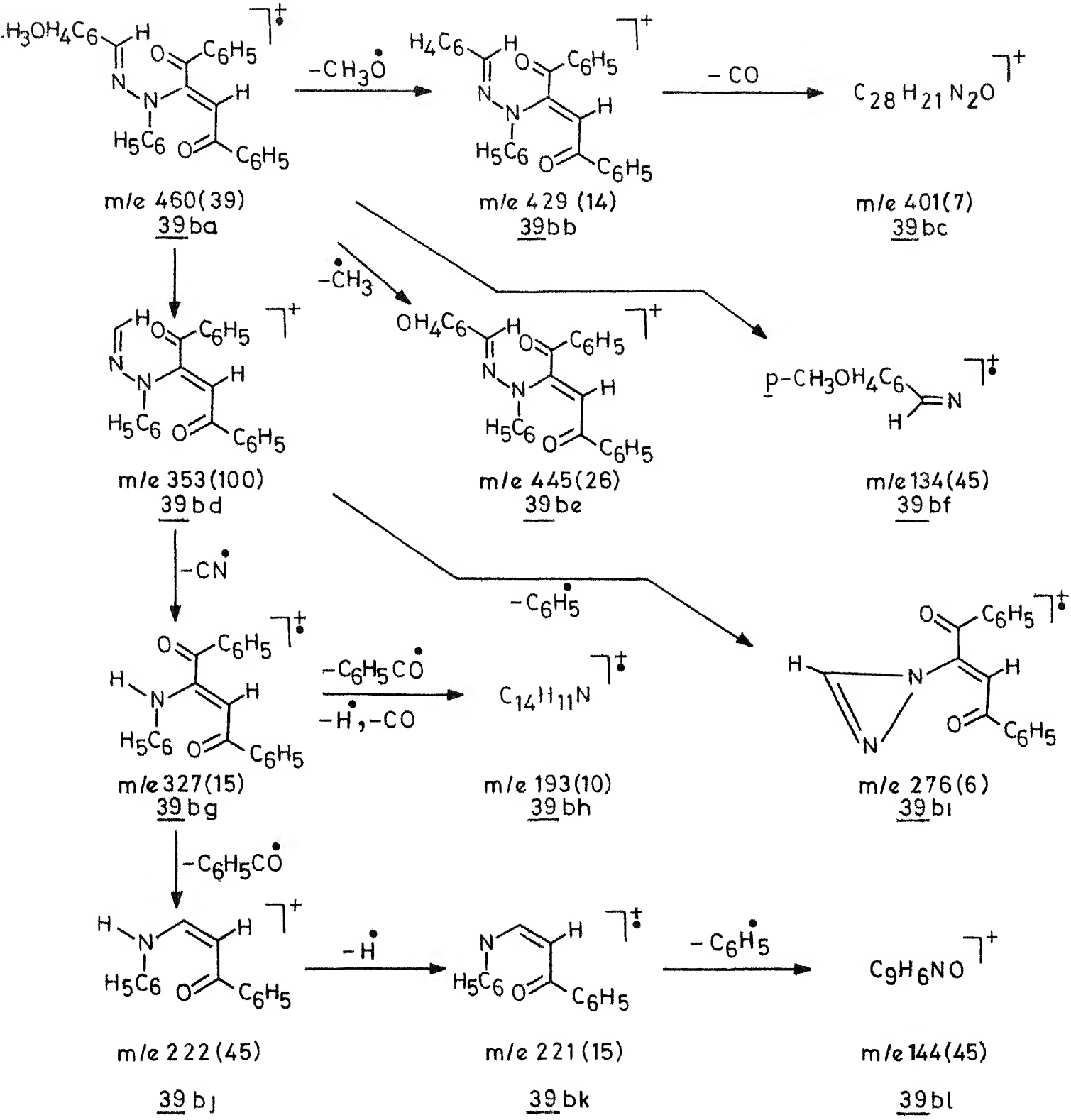
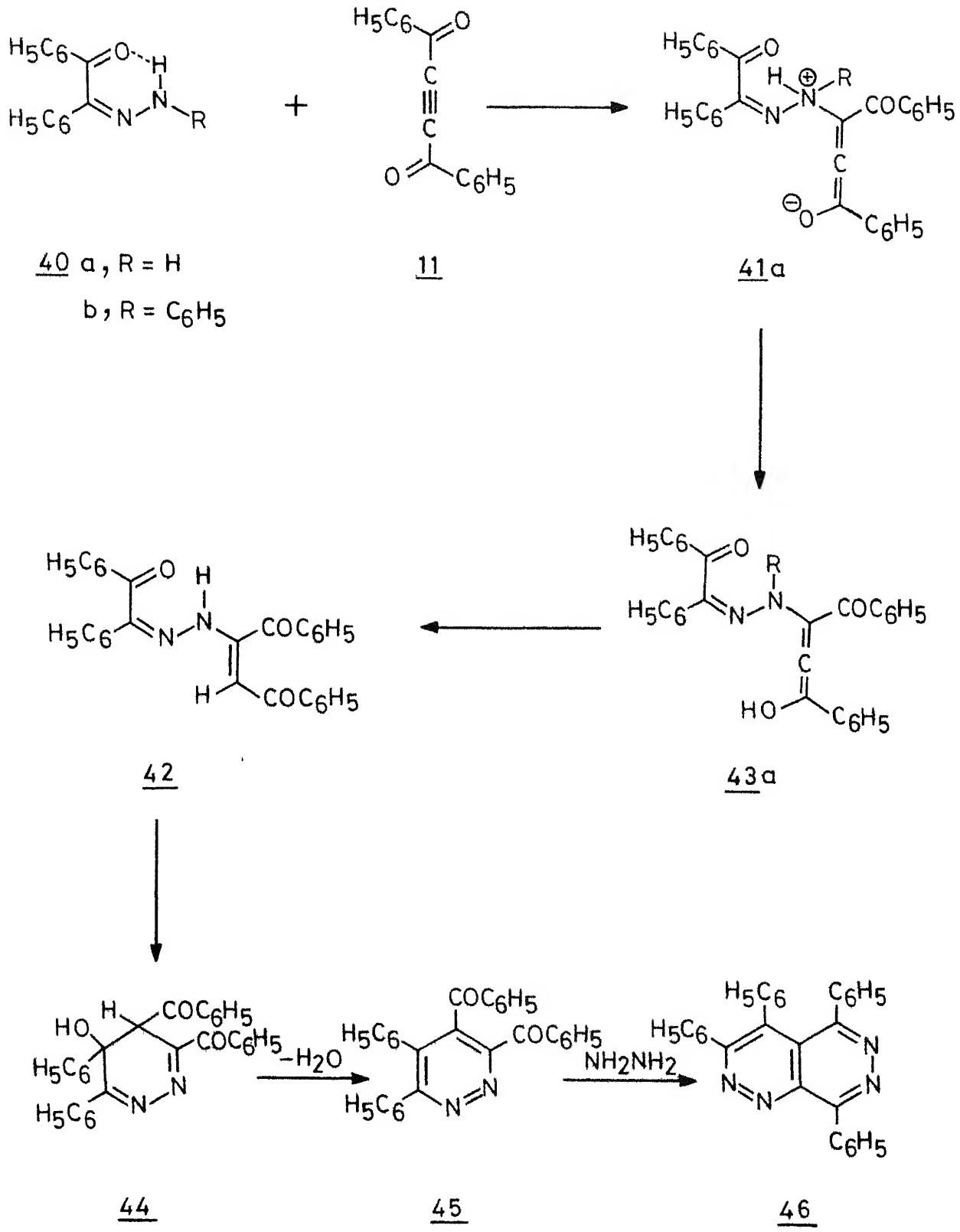


Fig. II . 15 Mass spectrum of 39 b

Scheme II 14


-CH3O
- CO
C28H21N2O
m/e 460(39)
39ba
m/e 429 (14)
39bb
m/e 401(7)
39bc
-CH3
p-CH3OH4C6
m/e 353(100)
39bd
m/e 445(26)
39be
m/e 134(45)
39bf
-CN
-C6H5
-C6H5CO
-H,-CO
C14H11N
m/e 327(15)
39bg
m/e 193(10)
39bh
m/e 276(6)
39bi
-C6H5CO
-H
-C6H5
C9H6NO
m/e 222(45)
39bj
m/e 221(15)
39bk
m/e 144(45)
39bl

Scheme II.15



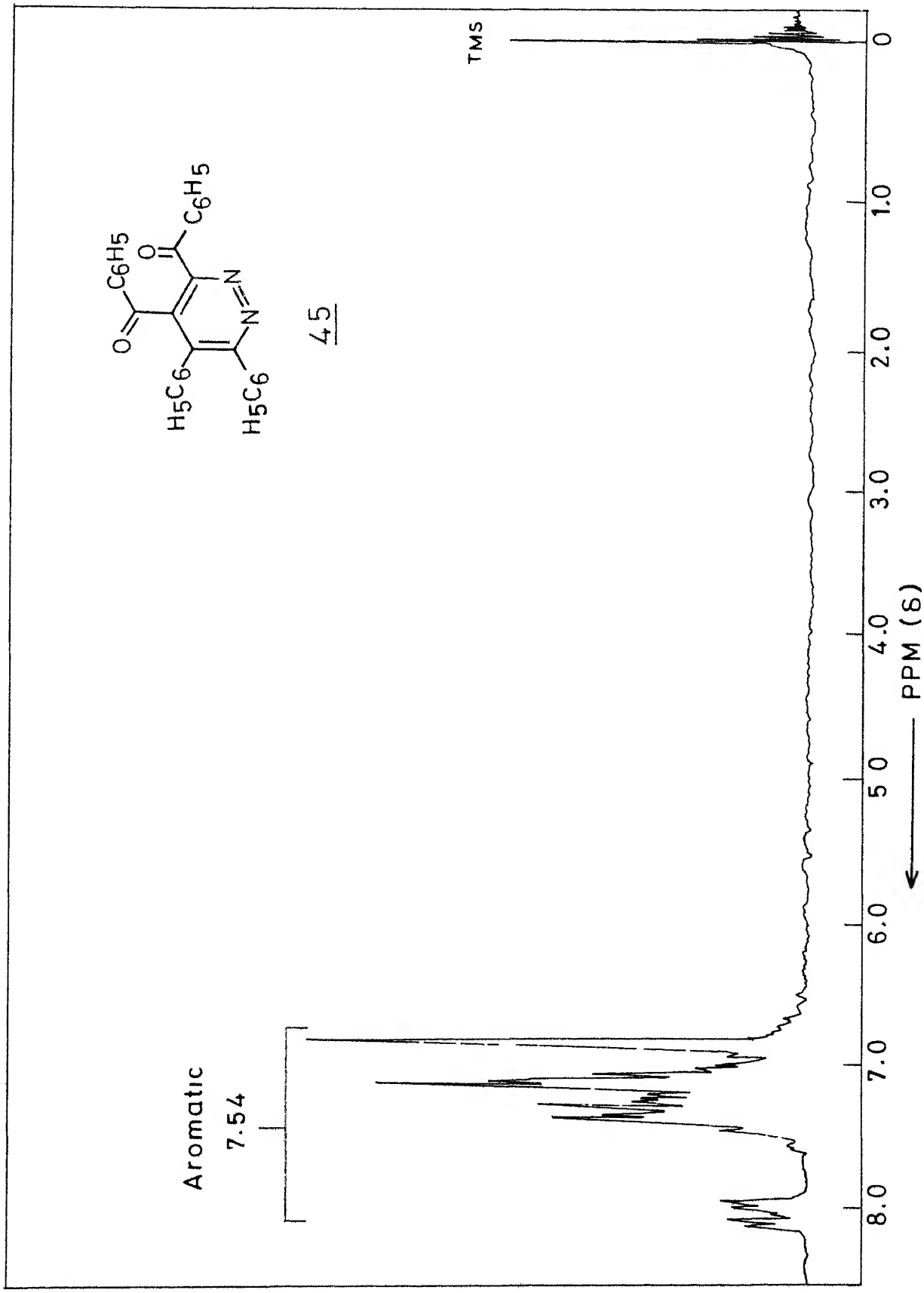


Fig II.16 NMR spectrum (60 MHz) of 45.

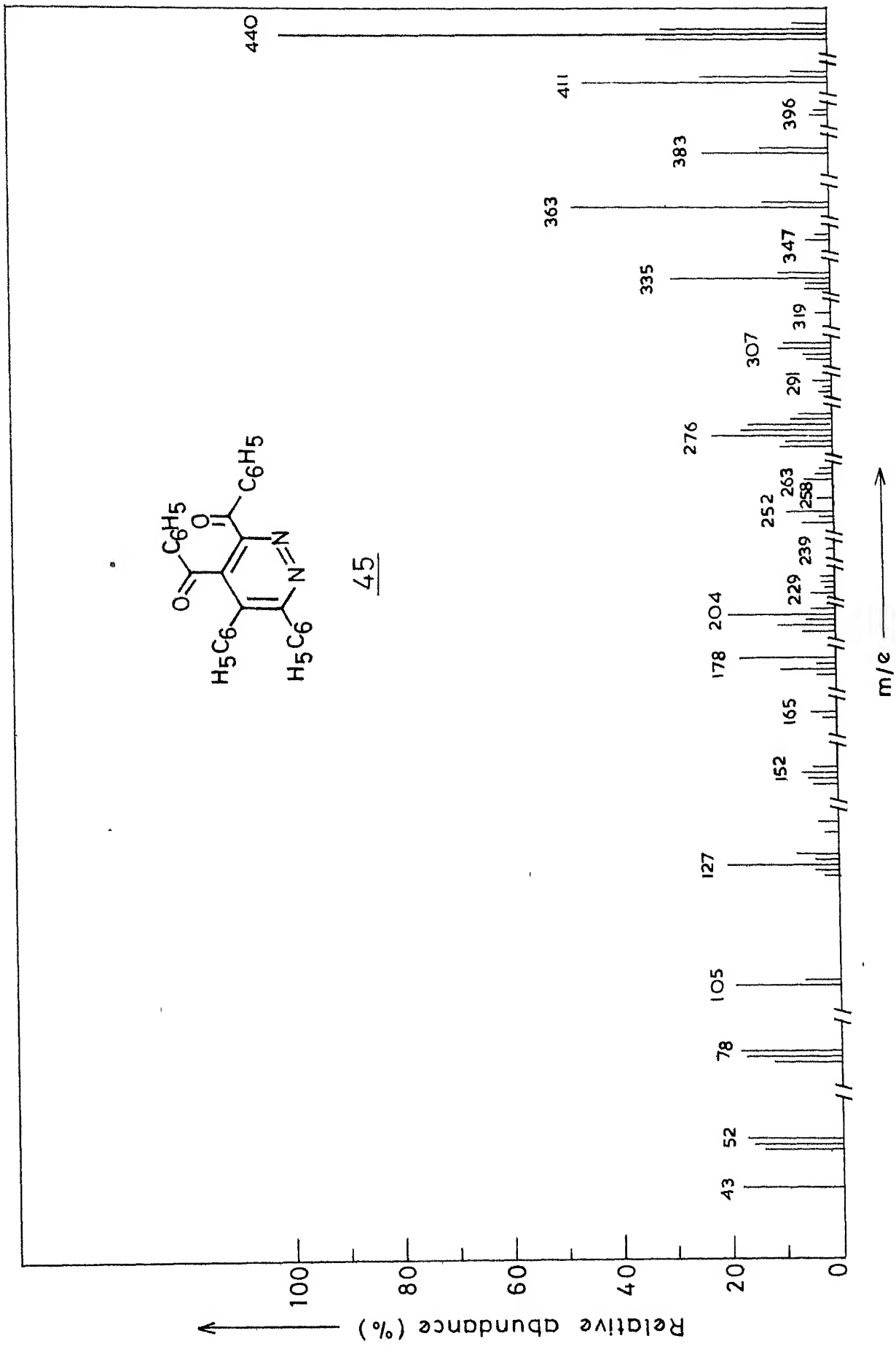


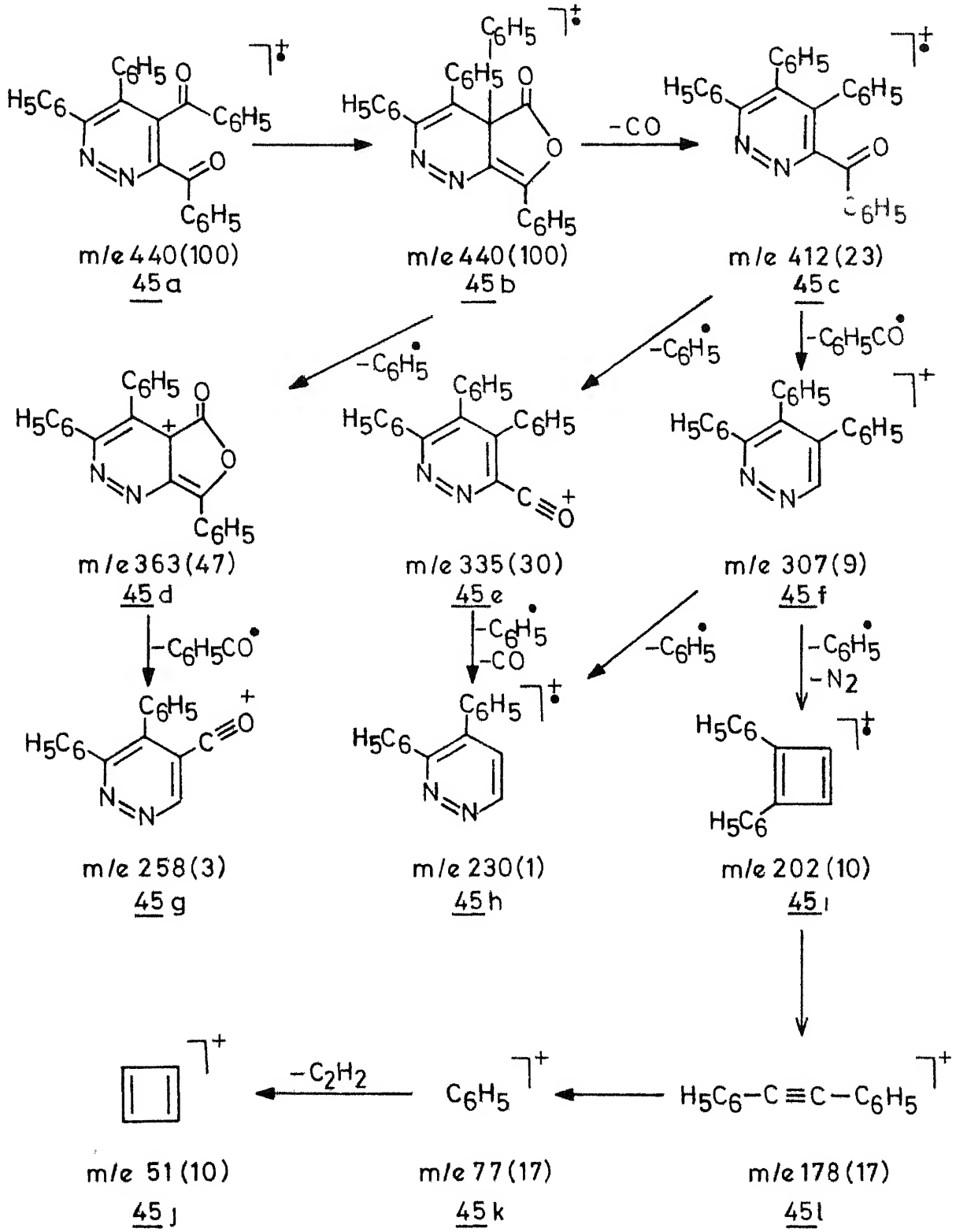
Fig. II.17 Mass spectrum of 45.

the spectrum were observed at m/e 439 (33), 412 (23), 411 (45), 396 (2), 383 (23), 363 (47), 335 (30), 319 (1), 307 (9), 306 (4), 291 (2), 278 (15), 277 (16), 276 (23), 258 (3), 230 (1), 229 (4), 204 (20), 202 (10), 201 (6), 178 (17), 105 (19), 77 (17) and 51 (10). Some of the probable fragmentation modes of 45 are shown in Scheme II.16 and Scheme II.17.

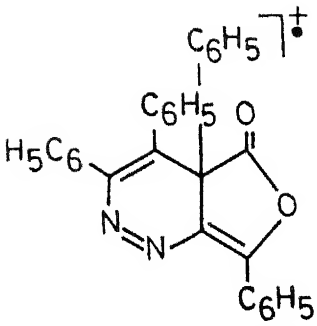
Further confirmation of the structure of 45 has been derived through its conversion to 3,4,5,8-tetraphenylpyridazino[4,5-c]pyridazine (46, 68%), on treatment with hydrazine. The structure of 46 was established on the basis of analytical results and spectral data. The IR spectrum of 46, for example, did not show any carbonyl absorption band. The NMR spectrum of 46 (Fig. II.18) showed a complex multiplet centred around δ 7.46 due to the aromatic protons. The mass spectrum of 46 (Fig. II.19) showed a molecular ion peak at m/e 436 (100). Other peaks were observed at m/e 408 (90), 380 (5), 376 (10), 331 (18), 303 (18), 276 (5), 256 (3), 254 (3), 230 (4), 229 (8), 226 (2), 202 (86), 178 (23), 177 (20), 176 (30), 151 (15), 126 (11), 105 (21), 77 (23) and 51 (6). Some of the probable modes of fragmentation are shown in Scheme II.18.

A probable route to the formation of 45 in the reaction of 40a with DBA is shown in Scheme II.15. It is assumed that the initially formed 1:1 adduct 42 undergoes cyclization to give the intermediate 44, which then loses elements of water to form

Scheme II.16


m/e 440(100)
45 a
m/e 440(100)
45 b
m/e 412(23)
45 c
m/e 363(47)
45 d
m/e 335(30)
45 e
m/e 307(9)
45 f
m/e 258(3)
45 g
m/e 230(1)
45 h
m/e 202(10)
45 i
m/e 51(10)
45 j
m/e 77(17)
45 k
m/e 178(17)
45 l
-CO
-C6H5
-C6H5CO
-C6H5
-CO
-C6H5
-N2
-C2H2

Scheme II.17



m/e 440(100)

45b

$-H^{\bullet}$

$C_{30}H_{19}N_2O_2^{+}$

m/e 439(33)

45m

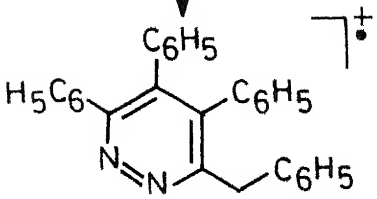
$-CO$

$C_{29}H_{19}N_2O^{+}$

m/e 411(45)

45n

$-CO_2$



m/e 396(2)

45o

$C_6H_5C\equiv O^{+}$

m/e 105(19)

45p

$-CO$

$C_{28}H_{19}N_2^{+}$

m/e 383(23)

45q

$-C_6H_5^{\bullet}$

$C_{23}H_{15}N_2^{+}$

m/e 319(1)

45r

$C_{22}H_{14}^{+\bullet}$

m/e 278(15)

45s

$-N_2$

$C_{22}H_{14}N_2^{+\bullet}$

m/e 306(4)

45t

$-N_2$

$C_{23}H_{15}^{+}$

m/e 291(12)

45u

$C_6H_5^{\bullet}$

$C_{16}H_9^{+}$

m/e 201(6)

45v

$-H^{\bullet}$

$-N_2$

$-H^{\bullet}$

$C_{22}H_{13}^{+}$

m/e 277(16)

45w

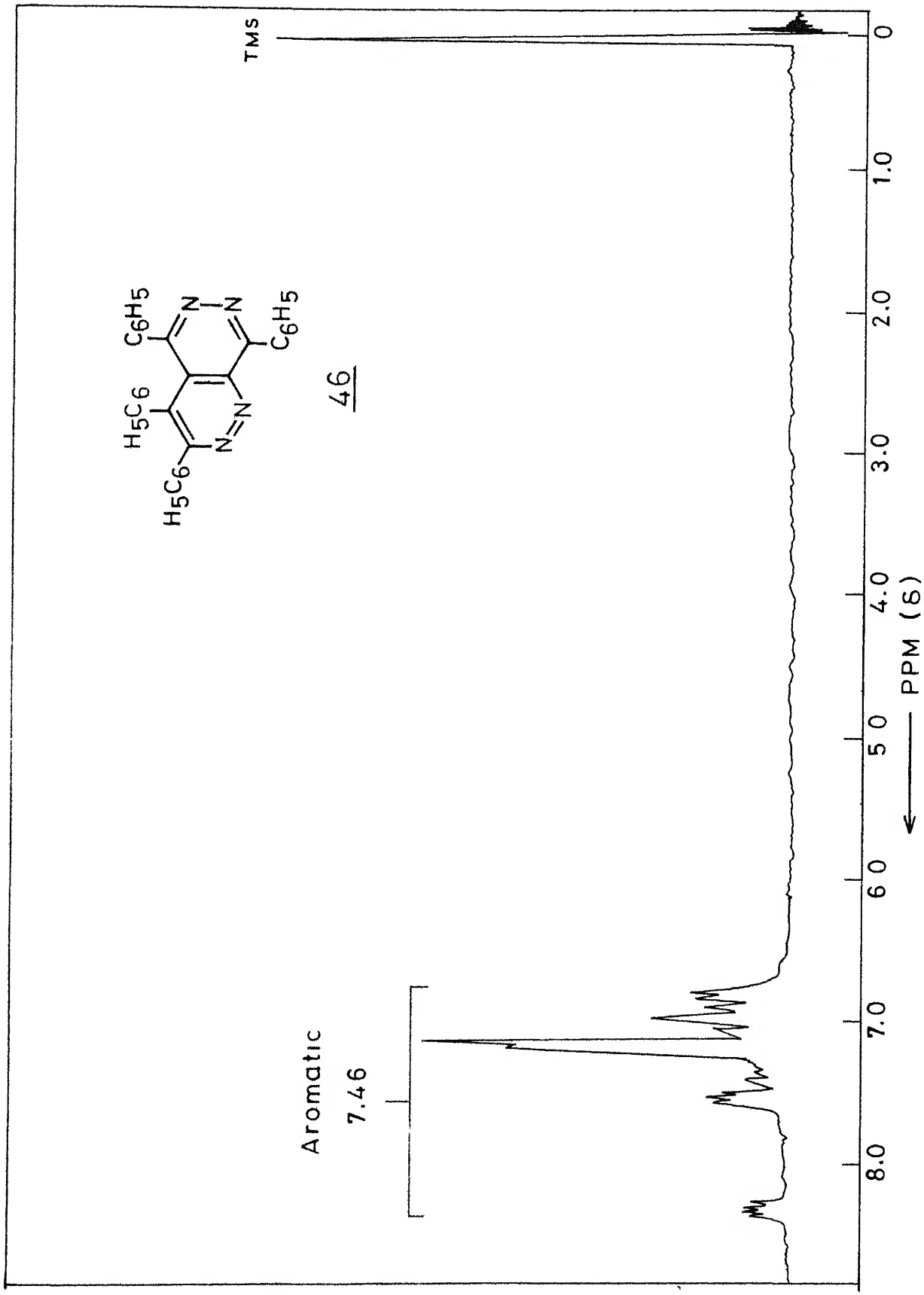


Fig. II. 18 NMR spectrum (100 MHz) of 46.

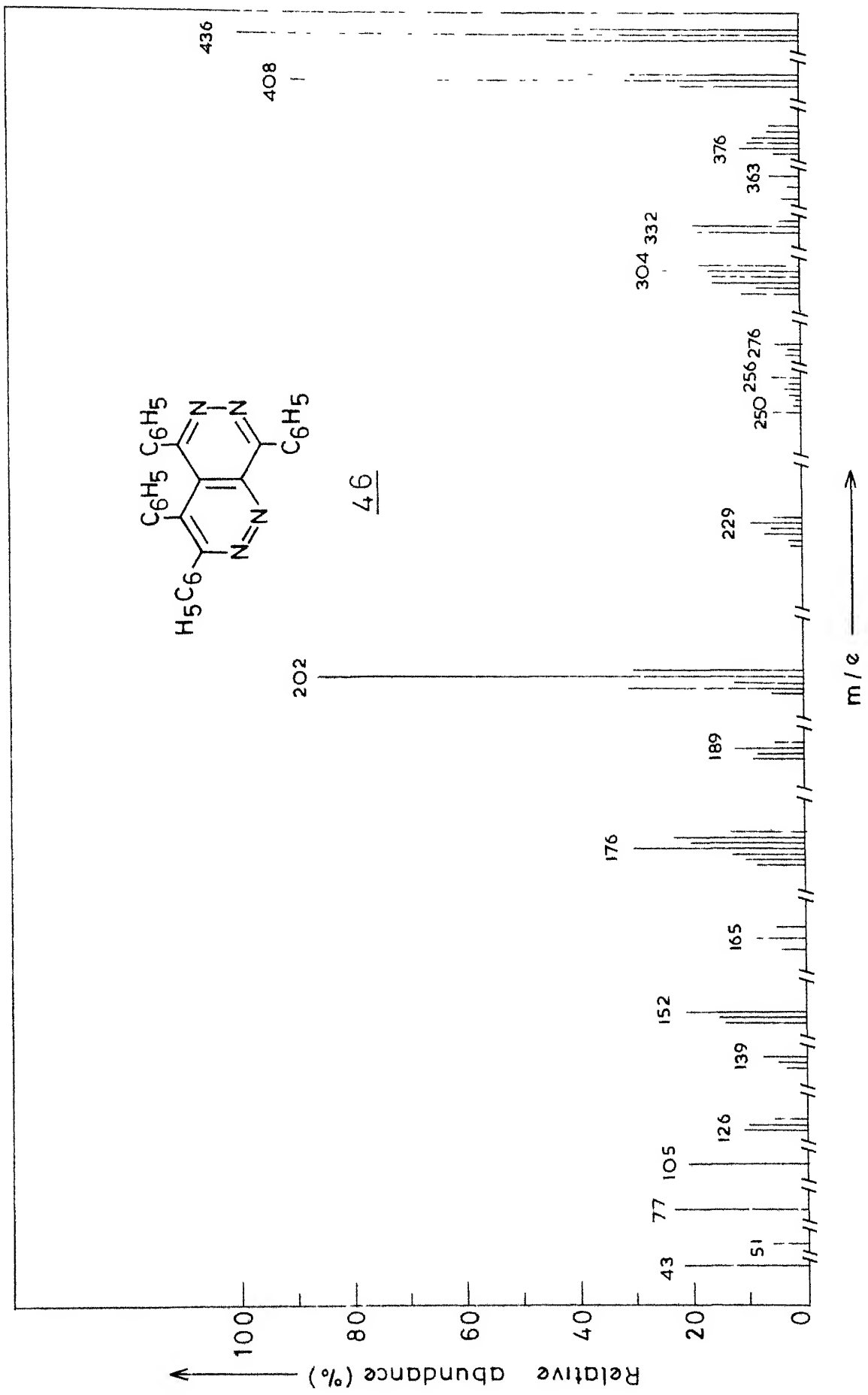
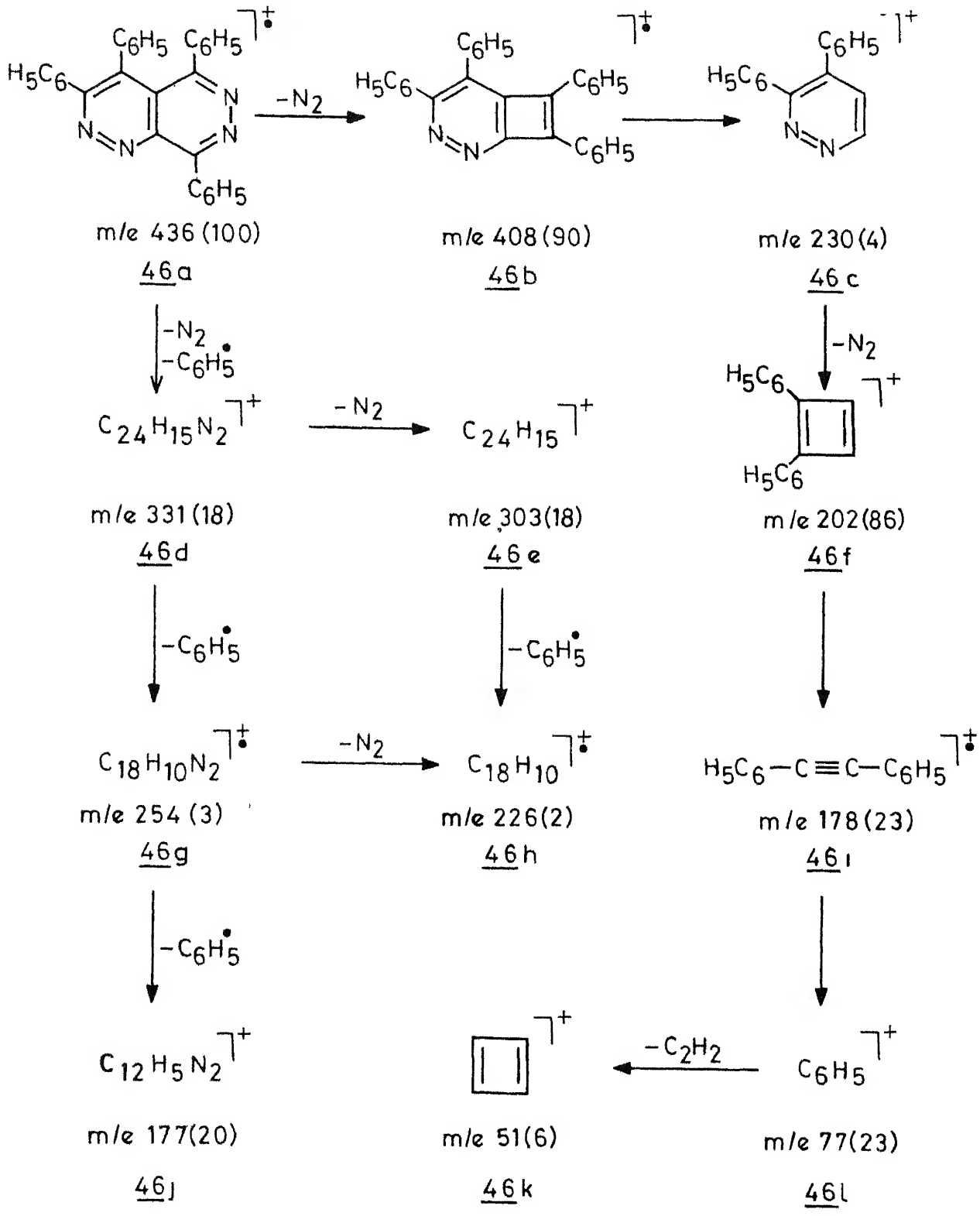


Fig. II .19 Mass spectrum of 46.

Scheme II.18

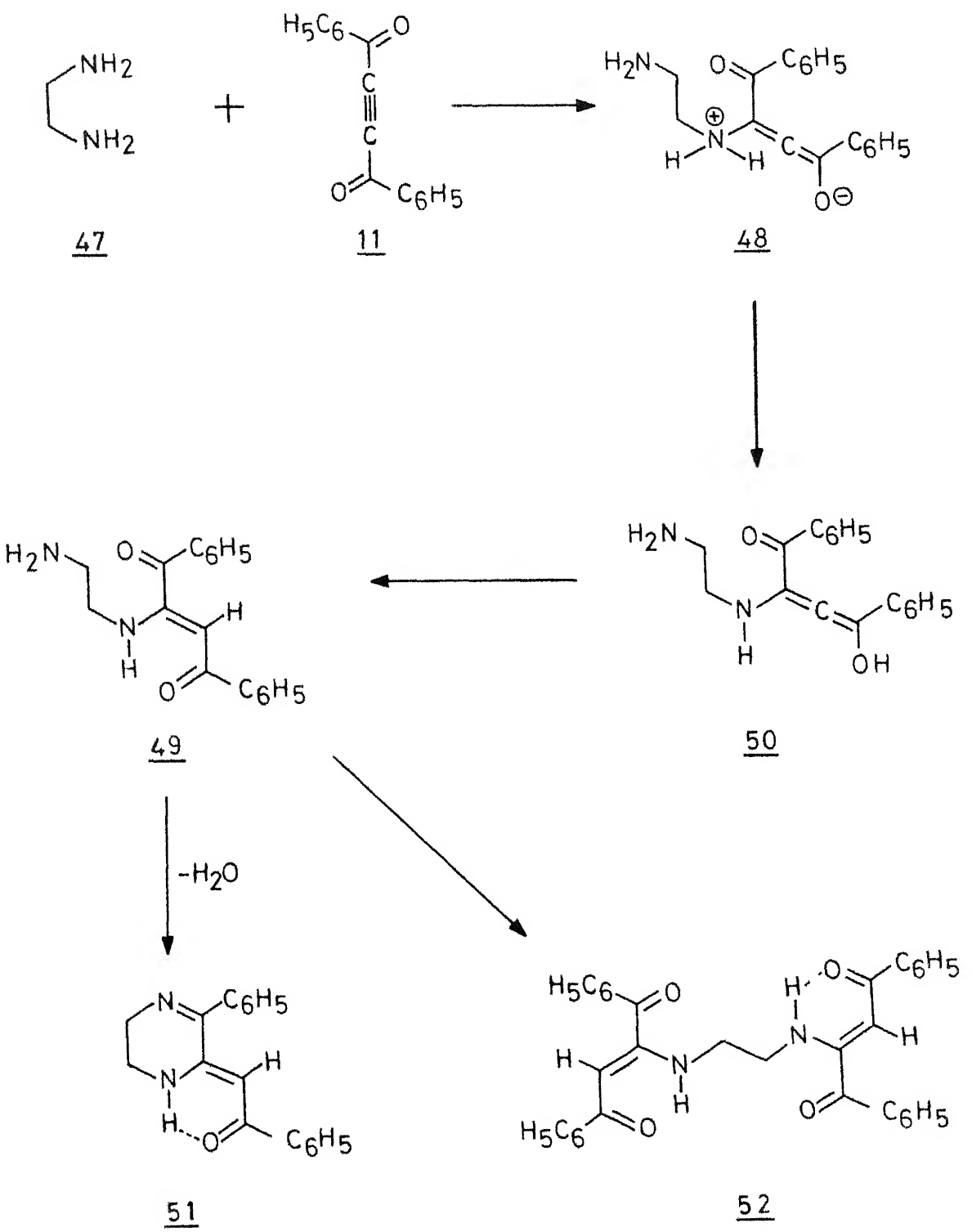

m/e 436 (100)
46a
m/e 408 (90)
46b
m/e 230 (4)
46c
m/e 331 (18)
46d
m/e 303 (18)
46e
m/e 202 (86)
46f
m/e 254 (3)
46g
m/e 226 (2)
46h
m/e 178 (23)
46i
m/e 177 (20)
46j
m/e 51 (6)
46k
m/e 77 (23)
46l

the pyridazino derivative 45. In support of this assumption, it has been observed that when the reaction of 40a with DBA was carried out in methanol at room temperature, a 23% yield of 2-(N-(1',2'-diaza-3',4'-diphenyl-4'-oxobut-2'-ene))-1,4-diphenyl but-2-ene-1,4-dione (42) was isolated, along with a 68% yield of 45. Further, it has been observed that 42 could be converted to the pyridazine 45, by refluxing in benzene.

In contrast to the reaction of benzil monohydrazone with DBA, it has been observed that practically no reaction occured when benzil monophenylhydrazone (40b) was treated with DBA in either refluxing methanol or xylene.

It has been reported earlier[15] that the reaction of ethylene diamine (47) with DBA leads to a tetrahydropyrazine derivative, whereas, open chain 1:2 adducts are formed in the reaction of 47 with acetylphenylacetylene.[16] In the present studies we have reinvestigated the reaction of ethylenediamine with DBA to examine the types of products formed in this case. Treatment of an equimolar mixture of 47 and DBA in methanol at room temperature gave a mixture of products consisting of 2-(2'-oxo-2'-phenylethylidene)-3-phenyl-1,2,5,6-tetraphenyl-pyridazine (51, 69%) and N,N'-bis-(2'-(1',4'-diphenylbut-2'-e-ne-1',4'-dione))-1,2-diaminoethane (52, 31%), whereas in THF at room temperature, a 18% yield of 51 and 76% yield of 52 were obtained (Scheme II.19). The structures of both 51 and 52 have

Scheme II.19



47 11 48

50

49

51 52

been established on the basis of analytical results and spectral data. The IR spectrum of 51, for example, showed an NH band at 3240 cm^{-1} and a strongly hydrogen-bonded carbonyl absorption at 1625 cm^{-1}. By concentration dependent IR studies in chloroform, it has been shown that the NH group in 51 is intramolecularly hydrogen-bonded. The NMR spectrum of 51 (Fig. II.20) showed two multiplets centred around δ 3.49 (2 H) and 3.93 (2 H) respectively, which have been assigned to the methylene protons. The vinylic proton appeared as a sharp singlet at δ 6.50 (1 H), whereas the aromatic protons appeared as a complex multiplet centred around δ 7.56 (10 H). The broad signal at δ 11.23 (1 H) which was exchangeable with D_2O, has been assigned to the NH proton.

Further evidence for the structure of 51 has been derived from its mass spectrum (Fig. II.21), which showed a molecular ion peak at m/e 276 (100). Other peaks in the spectrum were observed at m/e 275 (23), 258 (28), 248 (43), 220 (1), 219 (5), 199 (9), 171 (53), 145 (91), 131 (8), 117 (9), 115 (10), 105 (60), 103 (57), 102 (64), 101 (24), 77 (48) and 51 (12). Some of the probable modes of fragmentation are shown in Scheme II.20.

Likewise, the IR spectrum of 52 showed a band at 3200 cm^{-1}, characteristic of a hydrogen-bonded NH group and two carbonyl absorptions at 1680 and 1670 cm^{-1}, respectively. The

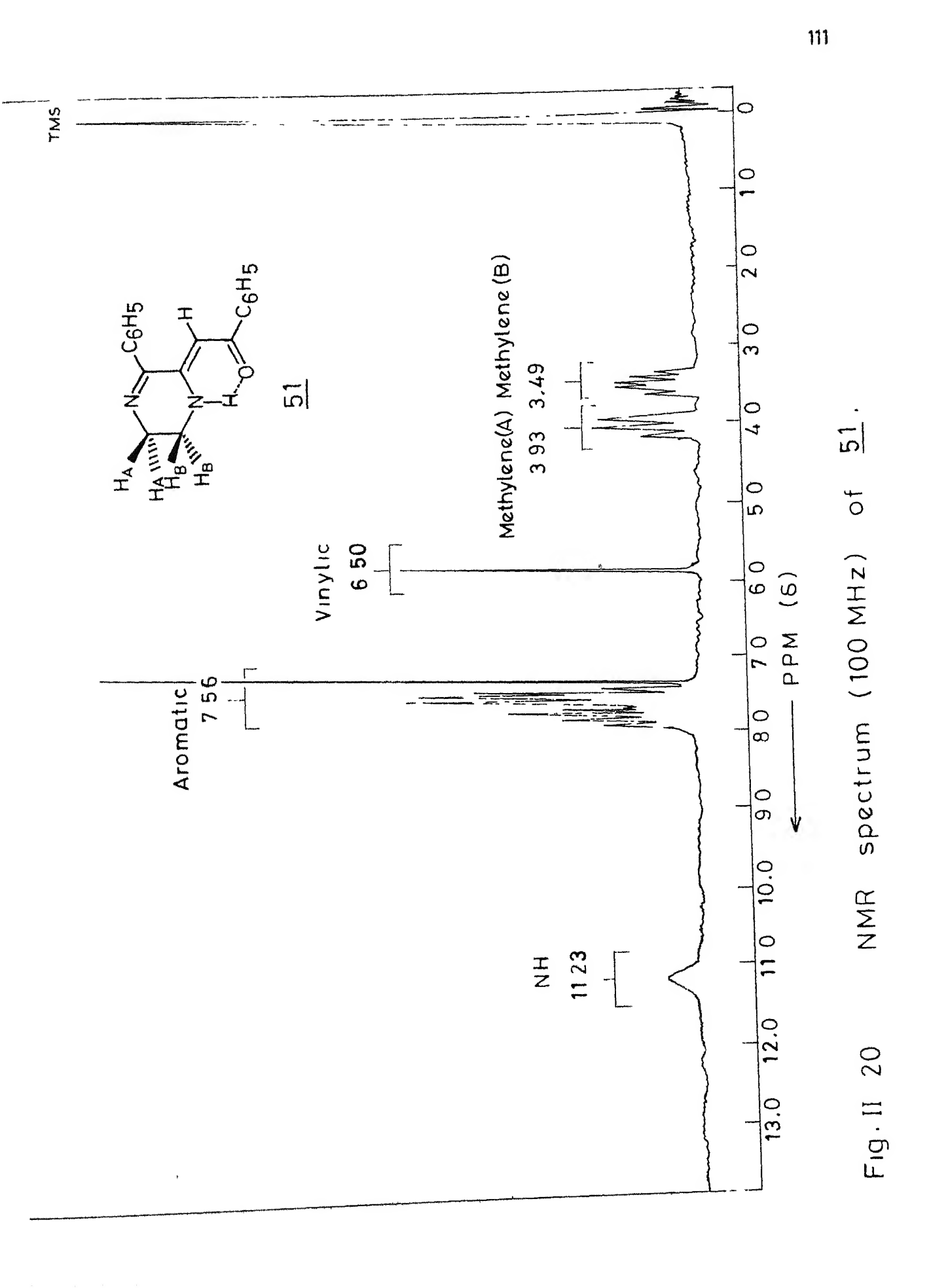


Fig. II 20 NMR spectrum (100 MHz) of 51.

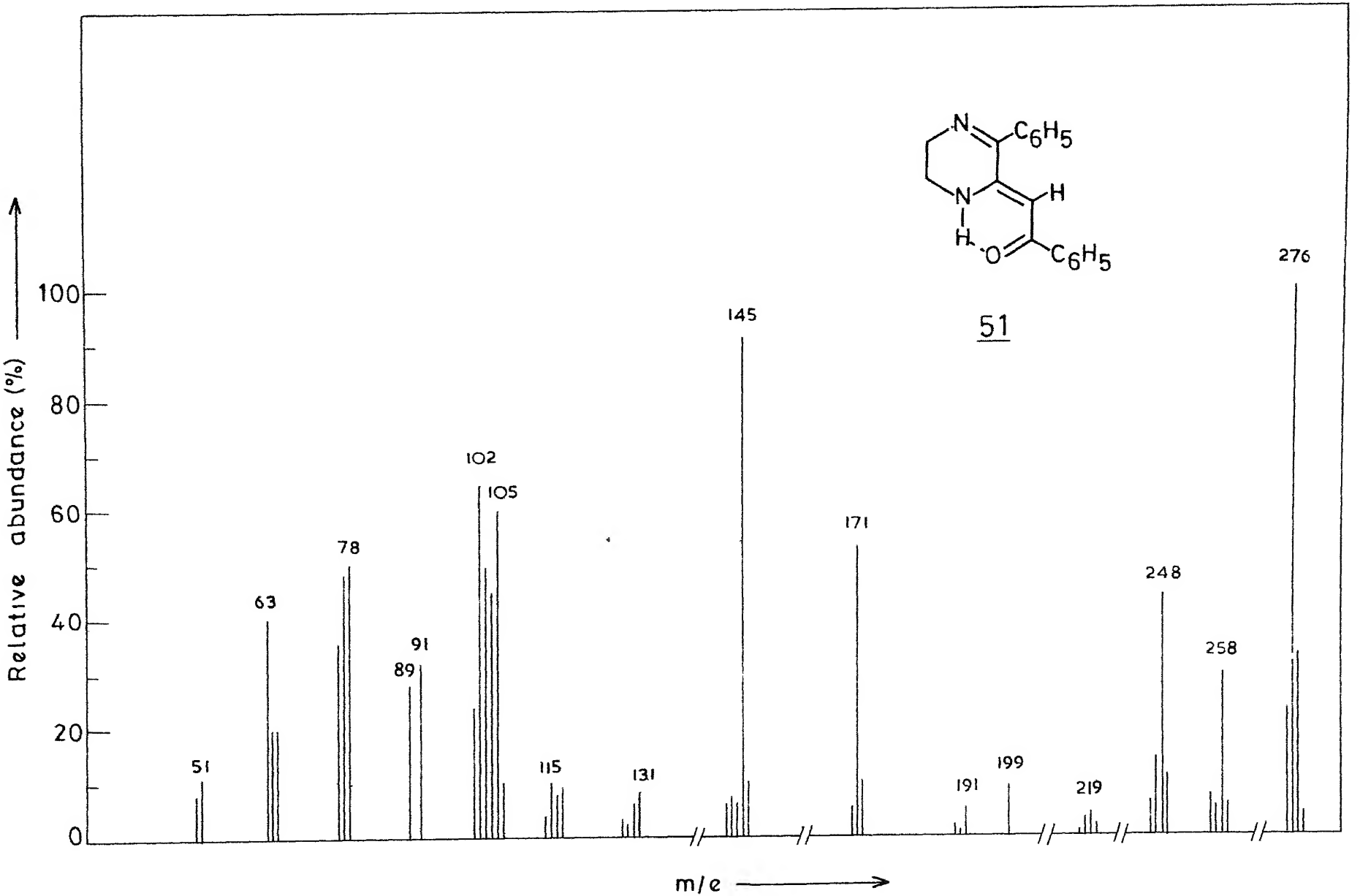
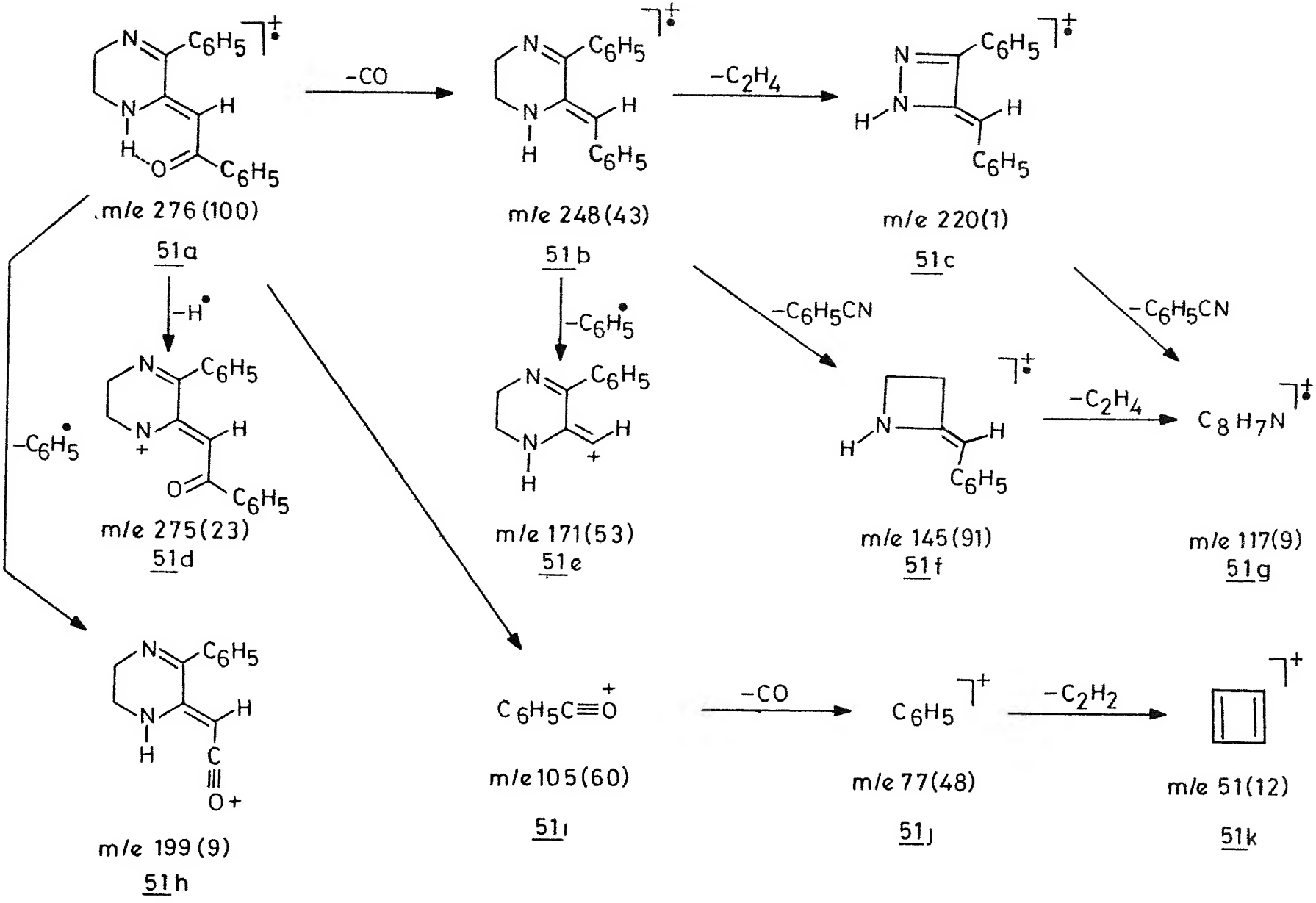


Fig. II .21 Mass spectrum of 51.

Scheme II.20


-CO
-C2H4
m/e 276 (100)
51a
m/e 248 (43)
51b
m/e 220 (1)
51c
-H•
-C6H5•
-C6H5CN
-C6H5CN
-C6H5•
m/e 275 (23)
51d
m/e 171 (53)
51e
m/e 145 (91)
51f
-C2H4
C8H7N+•
m/e 117 (9)
51g
m/e 199 (9)
51h
C6H5C≡O+
m/e 105 (60)
51i
-CO
C6H5+
m/e 77 (48)
51j
-C2H2
m/e 51 (12)
51k

NMR spectrum of 52 (Fig. II.22) showed a doublet at δ 3.46 (4 H, J = 10 Hz), a singlet at δ 5.78 (2 H), a multiplet centred around δ 7.73 (20 H) and a broad triplet centred around δ 10.86 (2 H, J = 10 Hz). It has been observed that on D_2O-shake, the broad triplet around δ 10.86 disappeared, whereas the doublet at δ 3.46 coalesced into a singlet, indicating thereby that the broad triplet could be assigned to the NH protons, whereas, the doublet at δ 3.46 could be assigned to the methylene protons. The singlet at δ 5.78 (2 H) has been assigned to the vinylic protons, whereas the complex multiplet around δ 7.73 has been assigned to the aromatic protons

Further support for the structure of 52 has been derived from its mass spectrum (Fig. II.23), which showed a molecular ion peak at m/e 528 (20). Other peaks were observed at m/e 510 (10), 477 (5), 423 (100), 405 (8), 352 (2), 318 (1), 300 (1), 264 (12), 236 (3), 213 (1), 172 (12), 160 (19), 159 (9), 131 (8), 105 (54), 91 (47), 77 (52) and 51 (6). Some of the possible modes of fragmentation of 52 are shown in Scheme II.21.

The formation of products such as 51 and 52 in the reaction of ethylenediamine (47) with DBA can be rationalized in terms of the pathways shown in Scheme II.19.

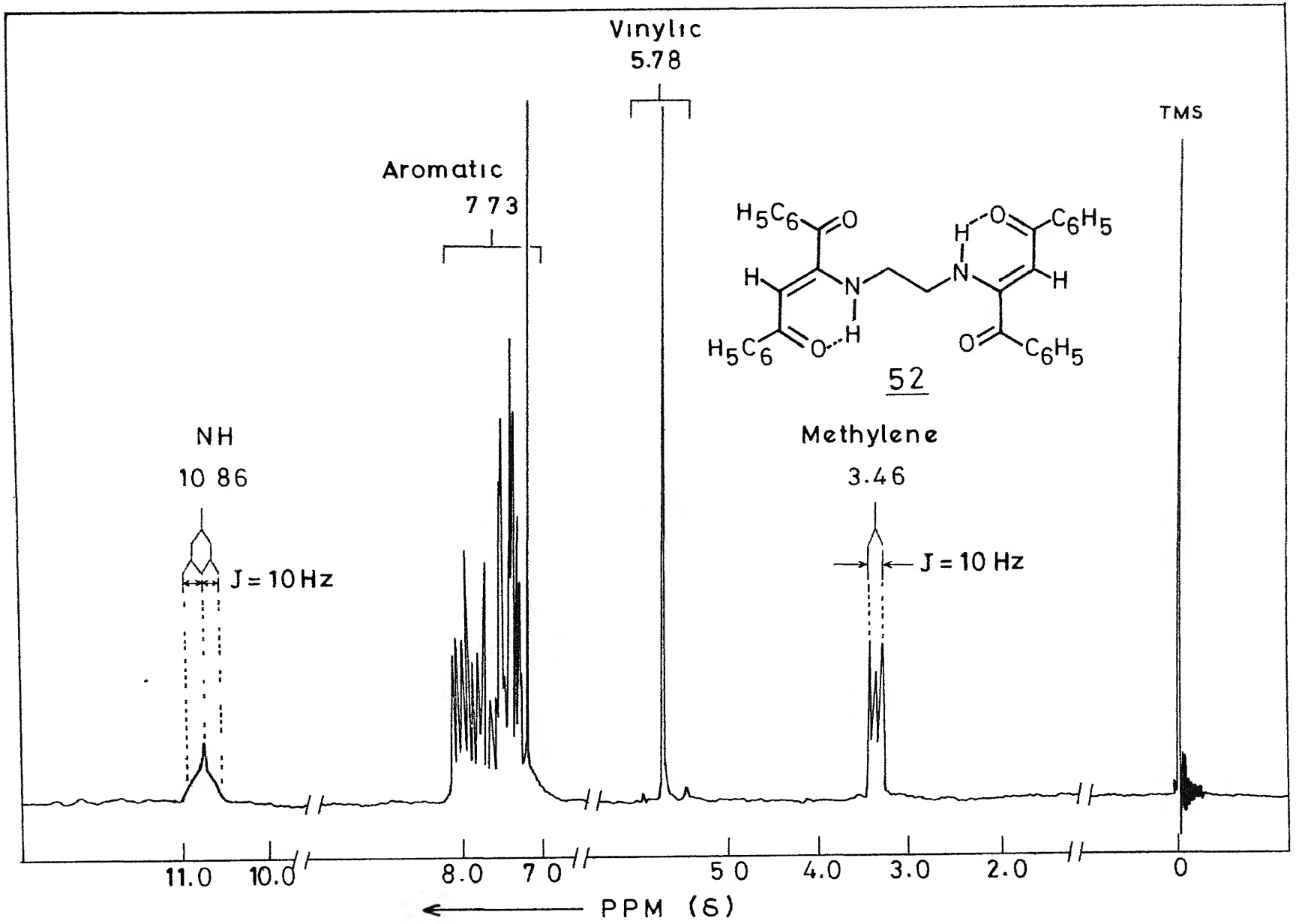


Fig II.22 NMR spectrum (100 MHz) of 52

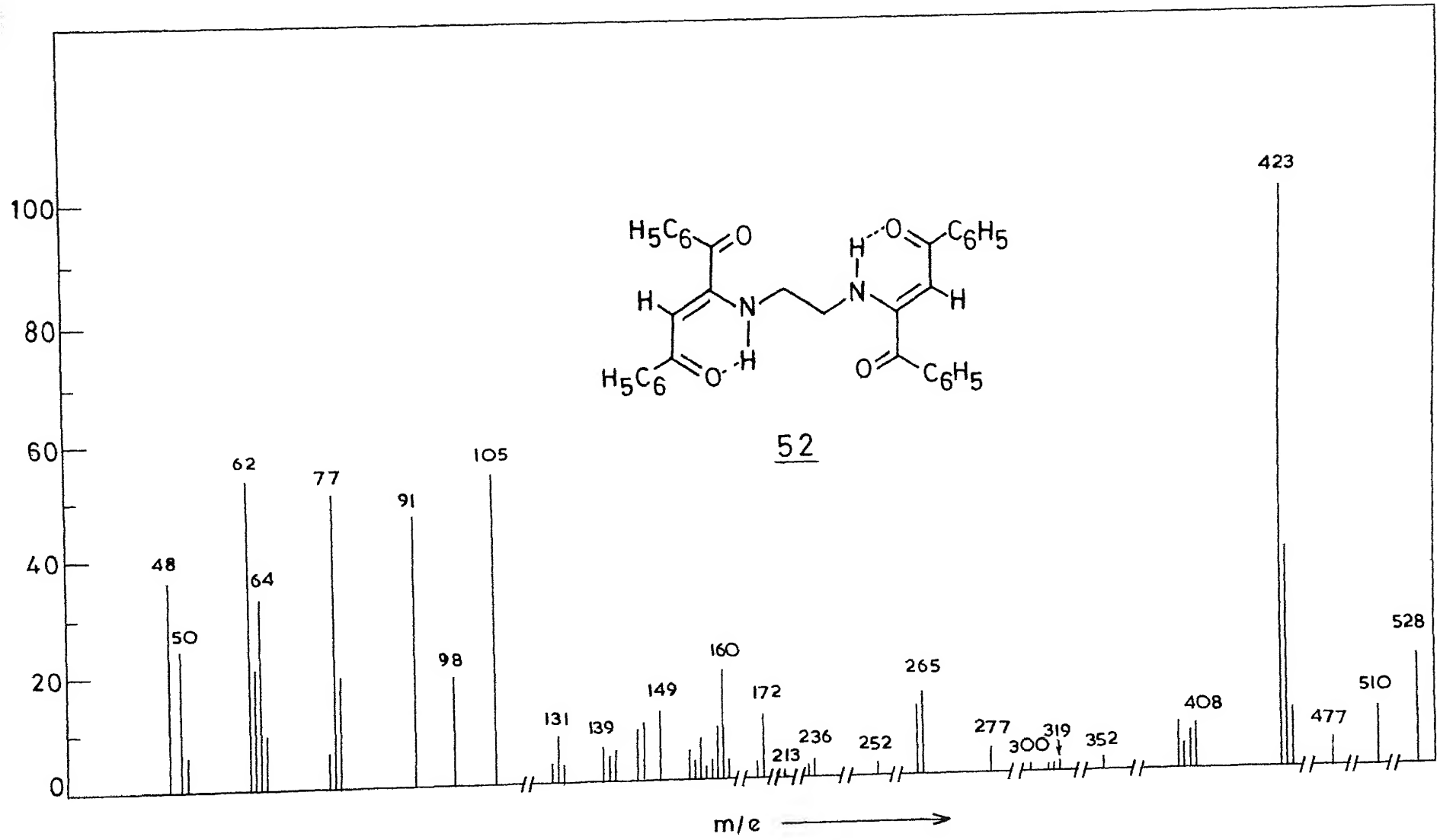
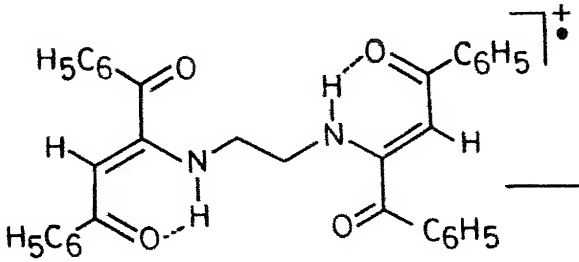


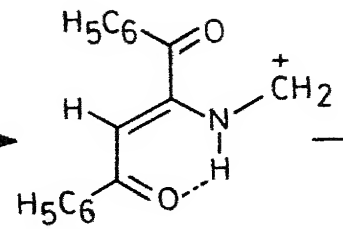
Fig. II.23 Mass spectrum of 52.

Scheme II.21



m/e 528 (20)

52a



m/e 264 (12)

52b

$C_{16}H_{14}NO^{+}$ m/e 236 (3)

52c

$C_6H_5C{\equiv}O^{+}$ m/e 105 (54)

52d

$C_{27}H_{23}N_2O_3^{+}$ m/e 423 (100)

52e

$C_{34}H_{26}N_2O_3^{+\cdot}$ m/e 510 (10)

52f

$C_{10}H_9NO^{+\cdot}$ m/e 159 (9)

52g

$C_9H_9N^{+\cdot}$ m/e 131 (8)

52h

$C_{20}H_{18}N_2O_2^{+\cdot}$ m/e 318 (1)

52i

$C_{13}H_{13}N_2O^{+}$ m/e 213 (1)

52j

$C_{27}H_{21}N_2O_2^{+}$ m/e 405 (8)

52k

$C_{20}H_{16}N_2O^{+\cdot}$ m/e 300 (1)

52l

II.4 EXPERIMENTAL

All melting points are uncorrected and were determined on a Mel-Temp, melting-point apparatus. The IR spectra were recorded on Perkin-Elmer Model 377 or 580 infrared spectrophotometers. The electronic spectra were recorded on a Beckmann DB or Cary-17D spectrophotometer. NMR traces were recorded on a Varian A-60, XL-100, HA-100 or Jeol 100 MHz spectrophotometers. The mass spectra were recorded on a Hitachi RMU-6E single focussing mass spectrometer or a Varian Mat CH7 mass spectrometer at 70 eV.

II.4.1 Starting Materials

Benzoylhydrazine (10),[17] mp 116-117°, benzoylphenylhydrazine (18),[18] mp 168°, ethyl N,C-diphenylglycinate (25),[19] mp 82°, benzaldehyde hydrazone (29a),[20] bp 140° (14 mm), benzophenone hydrazone (29b),[21] mp 98°, benzaldehyde phenylhydrazone (34a),[22] mp 156°, p-anisaldehyde phenylhydrazone (34b),[23] mp 121°, benzil monohydrazone (40a),[24] mp 151° (d), benzil monophenylhydrazone (40b),[25] mp 135° and dibenzoylacetylene (11),[26] mp 111° were prepared by reported procedures. Ethylenediamine (47), bp 116.5° (760 mm), obtained commercially was purified before use. Petroleum ether used was the fraction, bp 60-80°.

II.4.2 Reaction of Benzoylhydrazine (10) with Dibenzoylacetylene (11)

A In Tetrahydrofuran at Room Temperature

A mixture of benzoylhydrazine (10, 0.136 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was stirred at room temperature for a period of 4 hr. Removal of the solvent under vacuum gave an oily residue, which solidified on treatment with a small amount of methanol. Recrystallization of this product from methanol gave 0.34 g (92%) of 2-(2'-benzoylhydrazono)-1,4-diphenylbutan-1,2,4-trione (13), mp 100-101°.

Anal. Calcd for $C_{23}H_{18}N_2O_3$: C, 74.59; H, 4.86; N, 7.56; Mol. wt., 370. Found: C, 74.57; H, 4.56; N, 7.51; Mol. wt., 370 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3444 (ν_{N-H}), 3040 (ν_{C-H}, aromatic), 2950 and 2920 (ν_{CH_2}, asymmetric and symmetric), 1664 and 1644 ($\nu_{C=O}$), 1610 ($\nu_{C=N}$), 1574 and 1454 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 300 nm (ε, 13,200).

B In Methanol at Room Temperature

A mixture of 10 (0.136 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was stirred at room temperature for a period of 4 hr. Removal of the solvent under vacuum and recrystallization of the resultant residue from methanol gave

0.33 g (90%) of 2-(2'-benzoylhydrazono)-1,4-diphenylbutan-1,2,4-trione (13), mp 100-101° (mixture melting point).

C In Toluene Under Refluxing Conditions

A mixture of 10 (0.136 g, 1 mmol) and DBA (0.234 g, 1 mmol) in toluene (20 ml) was refluxed for 8 hr. Subsequent work-up in the usual manner gave 0.34 g (92%) of 2-(2'-benzoylhydrazono)-1,4-diphenylbutan-1,2,4-trione (13), mp 100-101° (mixture melting point), after recrystallization from methanol.

II.4.3 Acid-Hydrolysis of 2-(2'-Benzoylhydrazono)-1,4-diphenylbutan-1,2,4-trione (13)

A Using Methanolic Hydrochloric Acid

A mixture of 13 (0.2 g, 0.54 mmol) and concentrated hydrochloric acid (1 ml) in methanol (10 ml) was refluxed for 2 hr. Removal of the solvent under vacuum gave a sticky mass, which was dissolved in ether, washed with water and subsequently dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a solid, which on fractional crystallization from methanol gave 0.14 g (95%) of 5-benzoyl-3-phenylpyrazole (17), mp 170° (mixture melting point)[7] and 40 mg (70%) of benzoic acid, mp 122° (mixture melting point).

B Using Orthophosphoric Acid

A mixture of 13 (0.5 g, 1.35 mmol) and orthophosphoric acid (6 ml) was heated around 100-105° for 2 hr. Treatment of the reaction mixture with water and neutralization with sodium hydroxide gave a product which was extracted with ether. The ether-extract was dried over anhydrous sodium sulfate. Removal of the solvent under vacuum gave 0.3 g (90%) of 5-benzoyl-3-phenylpyrazole (17), mp 170° (mixture melting point).[7]

The aqueous layer was acidified with dilute hydrochloric acid and extracted with methylene chloride to give 0.1 g (60%) of benzoic acid, mp 122° (mixture melting point).

II.4.4 Reaction of Benzoylphenylhydrazine (18) with Dibenzoylacetylene (11)

A In Methanol Under Refluxing Conditions

A mixture of benzoylphenylhydrazine (18, 0.212 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was refluxed for 3 hr, during which period a solid precipitated. This solid material was filtered off and recrystallized from ethanol to give 0.4 g (89%) of 2-(2'-benzoyl-1'-phenylhydrazo)-1,4-diphenyl-but-2-ene-1,4-dione (20), mp 240-241°.

Anal. Calcd for $C_{29}H_{22}N_2O_3$: C, 78.03; H, 4.93; N, 6.28; Mol. wt., 446. Found: C, 78.28; H, 4.77; N, 6.30; Mol. wt., 446 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3260 (ν_{N-H}, intermolecularly hydrogen-bonded), 3050 (ν_{C-H}, aromatic), 1695 and 1670 ($\nu_{C=O}$), 1620, 1595 and 1575 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 260 nm (ε, 20,100) and 340 (14,400).

B In Toluene Under Refluxing Conditions

A mixture of 18 (0.212 g, 1 mmol) and DBA (0.234 g, 1 mmol) was refluxed in toluene (20 ml) for 5 hr. The colourless solid that separated out during the reaction was filtered off and recrystallized from ethanol to give 0.36 g (80%) of 2-(2'-benzoyl-1'-phenylhydrazo)-1,4-diphenylbut-2-ene-1,4-dione (20), mp 240-241° (mixture melting point).

C In Tetrahydrofuran Under Refluxing Conditions

A mixture of 18 (0.212 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was refluxed for 24 hr. Work-up of the reaction mixture as in the earlier cases resulted in the isolation of 0.19 g (90%) of 18, mp 168° (mixture melting point) and 0.21 g (90%) of DBA, mp 111° (mixture melting point).

II.4.5 Attempted Cyclization of 2-(2'-Benzoyl-1'-phenylhydrazo)-1,4-diphenylbut-2-ene-1,4-dione (20) Using Orthophosphoric Acid

A mixture of 20 (0.446 g, 1 mmol) and orthophosphoric acid (6 ml) was heated around 130° for 2 hr. The reaction mixture was treated with water, neutralized with sodium hydroxide and extracted with ether. The ether-extract was dried over anhydrous sodium sulfate and the solvent was removed under vacuum to give a product which was chromatographed over silica gel. Elution with a mixture (3:7) of benzene and petroleum ether gave 0.26 g (80%) of 5-benzoyl-1,3-diphenylpyrazole (24), mp 100° (lit.[12] mp 98-100°), after recrystallization from methanol.

Anal. Calcd for $C_{22}H_{16}N_2O$: C, 81.47; H, 4.94; N, 8.65; Mol. wt., 324. Found: C, 81.56; H, 5.12; N, 8.50; Mol. wt., 324 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}), 1650 ($\nu_{C=O}$), 1595, 1575, 1520 and 1500 cm^{-1} ($\nu_{C=C}$).

UV spectrum (chloroform) λ_{max}: 258 nm (ε, 36,700) and 318 (3,400).

The aqueous layer was acidified with dilute hydrochloric acid and extracted with methylene chloride to give 85 mg (70%) of benzoic acid, mp 122° (mixture melting point), after recrystallization from a mixture (1:9) of benzene and petroleum ether.

II.4.6 Reaction of Ethyl N,C-Diphenylglycinate (25) with Dibenzoylacetylene

A In Methanol at Room Temperature

A mixture of ethyl N,C-diphenylglycinate (25, 0.255 g, 1 mmol) and DBA (0.234 g, 1 mmol) was stirred in methanol (20 ml) for 1 hr, during which period a yellow solid precipitated out. This material was filtered off and recrystallized from methanol to give 0.2 g (45%) of 2,3-dibenzoyl-4-hydroxy-1,5-diphenylpyrrole (27), mp 170°.

Anal. Calcd for $C_{30}H_{21}NO_3$: C, 81.28; H, 4.74; N, 3.16; Mol. wt., 443. Found: C, 80.82; H, 4.75; N, 3.29; Mol. wt., 443 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3320 (ν_{O-H}), 3045 (ν_{C-H}, aromatic), 1640 and 1620 ($\nu_{C=O}$), 1590, 1490 and 1462 cm^{-1} ($\nu_{C=C}$).

UV spectrum (95% ethanol) λ_{max}: 268 nm (ε, 14,100) and 400 (2,800).

Mass spectrum m/e (relative intensity): 443 (4) (M^+), 317 (2), 236 (7), 190 (11), 149 (18), 131 (6), 123 (7), 122 (10), 112 (5), 105 (100), 83 (72), 77 (41) and 51 (14).

The mother liquor, obtained after the removal of the solid product, was concentrated under reduced pressure to give an additional crop of 0.155 g (35%) of 27, mp 170° (mixture melting point), after recrystallization from methanol.

B In Tetrahydrofuran at Room Temperature

A mixture of 25 (0.255 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was stirred at room temperature for 1 hr. Subsequent work-up in the usual manner gave 0.4 g (90%) of 2,3-dibenzoyl-4-hydroxy-1,5-diphenylpyrrole (27), mp 170° (mixture melting point).

II.4.7 Reaction of Benzaldehyde Hydrazone (29a) with Dibenzoylacetylene (11)

A In Methanol at Room Temperature

A mixture of benzaldehyde hydrazone (29a, 0.12 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was stirred at room temperature for 1 hr, during which period a yellow solid separated out. This solid material was filtered off and recrystallized from a mixture (3:1) of chloroform and petroleum ether to give 0.31 g (88%) of 2-(1'-hydrazinyl-2'-benzylidene)-1,4-diphenyl-but-2-ene-1,4-dione (31a), mp 164°.

Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.96; H, 5.09; N, 7.91; Mol. wt., 354. Found: C, 78.05; H, 5.10; N, 7.88; Mol. wt., 354 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3090 (ν_{N-H}, intramolecularly hydrogen-bonded), 3060 (ν_{C-H}, aromatic), 1675 ($\nu_{C=O}$), 1610 ($\nu_{C=N}$), 1590, 1550 and 1450 cm^{-1} ($\nu_{C=C}$).

UV spectrum (95% ethanol) λ_{max}: 260 nm (ε, 20,000) and 390 (28,100).

B In Tetrahydrofuran at Room Temperature

A mixture of 29a (0.12 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was stirred at room temperature for ½ hr. Removal of the solvent under reduced pressure gave an oily mass, which solidified on treatment with a small amount of methanol. Recrystallization of this solid from a mixture (3:1) of chloroform and petroleum ether gave 0.22 g (62%) of 31a, mp 164° (mixture melting point).

II.4.8 Acid-Hydrolysis of 2-(1'-Hydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (31a) Using Methanolic Hydrochloric Acid

A mixture of 31a (0.3 g, 0.85 mmol) and concentrated hydrochloric acid (1 ml) in methanol (15 ml) was refluxed for 1 hr. Subsequent work-up, in the usual manner, gave 0.2 g (95%) of 5-benzoyl-3-phenylpyrazole (17), mp 170° (mixture melting point),[7] after recrystallization from methanol.

II.4.9 Reaction of Benzophenone Hydrazone (29b) with Dibenzoylacetylene (11)

A In Methanol at Room Temperature

A mixture of benzophenone hydrazone (29b, 0.196 g, 1 mmol) and DBA (0.234, 1 mmol) in methanol (20 ml) was stirred at room

temperature for ½ hr, during which period, a yellow solid precipitated out. This material was filtered off and recrystallized from a mixture (2:1) of benzene and petroleum ether to give 0.4 g (93%) of 2-(1'-hydrazinyl-2'-benzhydrylidene)-1,4-diphenyl-but-2-ene-1,4-dione (31b), mp 184-185°.

Anal. Calcd for $C_{29}H_{22}N_2O_2$: C, 80.93; H, 5.12; N, 6.51; Mol. wt., 430. Found: C, 80.77; H, 5.30; N, 6.48; Mol. wt., 430 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3160-2980 (ν_{N-H}, intramolecularly hydrogen-bonded and ν_{C-H}), 1675 ($\nu_{C=O}$), 1600, 1570 and 1540 cm^{-1} ($\nu_{C=C}$).

UV spectrum (95% ethanol) λ_{max}: 250 nm (ε, 21,000) and 395 (26,200).

B In Tetrahydrofuran Under Refluxing Conditions

A mixture of 29b (0.196 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was refluxed for 12 hr. Work-up of the reaction mixture in the usual manner resulted in the isolation of 0.175 g (90%) of the unchanged starting material (29b), mp 98° (mixture melting point) and 0.19 g (80%) of DBA, mp 111° (mixture melting point).

II.4.10 Acid-Hydrolysis of 2-(1'-Hydrazinyl-2'-benzhydrylidene)-1,4-diphenylbut-2-ene-1,4-dione (31b) Using Methanolic Hydrochloric Acid

A mixture of 31b (0.25 g, 0.58 mmol) and concentrated hydrochloric acid (1 ml) in methanol (15 ml) was refluxed for 4 hr. Work-up of the reaction mixture in the usual manner gave 0.14 g (98%) of 5-benzoyl-3-phenylpyrazole (17), mp 170° (mixture melting point).[7]

II.4.11 Reaction of Benzaldehyde Phenylhydrazone (34a) with Dibenzoylacetylene (11)

A mixture of benzaldehyde phenylhydrazone (34a, 1.17 g, 5 mmol) and DBA (0.98 g, 5 mmol) was refluxed in methanol (50 ml) for 6 hr, during which period a light yellow solid precipitated out. This solid material was filtered off and recrystallized from a mixture (3:1) of chloroform and petroleum ether to give 0.4 g of an unidentified compound 36, mp 250-251° (d).

Anal. Calcd for $C_{61}H_{42}N_2O_6$: C, 81.51; H, 4.67; N, 3.11; Found: C, 81.97; H, 4.57; N, 2.84.

IR spectrum (KBr) ν_{max}: 3060 and 3020 (ν_{C-H}), 1680 and 1655 ($\nu_{C=O}$), 1625 ($\nu_{C=N}$), 1595, 1580, 1520 and 1490 ($\nu_{C=C}$), 1450, 1380, 1260, 1220 and 700 cm^{-1}.

UV spectrum (chloroform) λ_{max}: 262 nm (ε, 40,400), 315 (15,700), 330 (14,400, sh) and 360 (10,200, sh).

NMR spectrum ($CDCl_3$): δ 2.30 (1 H, d, J = 12 Hz), δ 3.15 (1 H, d, J = 12 Hz), δ 5.16 (1 H, d, 6 Hz) and δ 7.33 (39 H, m, aromatic).

The mother liquor, obtained after the removal of 36, was concentrated under reduced pressure to give a product which was chromatographed over silica gel. Elution with a mixture (1:1) of benzene and petroleum ether gave 0.1 g (8%) of 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (38), mp 108° (mixture melting point),[27] after recrystallization from methanol.

Further elution of the column with benzene gave 0.4 g (19%) of 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (39a), mp 207°, after recrystallization from a mixture (2:1) of benzene and petroleum ether.

Anal. Calcd for $C_{29}H_{22}N_2O_2$: C, 80.93; H, 5.12; N, 6.51; Mol. wt., 430. Found: C, 80.84; H, 5.18; N, 6.65; Mol. wt., 430 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3045 (ν_{C-H}, aromatic), 1685 ($\nu_{C=O}$), 1600, 1585 and 1514 cm^{-1} ($\nu_{C=C}$).

UV spectrum (95% ethanol) λ_{max}: 263 nm (ε, 32,800) and 377 (46,800).

II.4.12 Reaction of p-Anisaldehyde Phenylhydrazone (34b) with Dibenzoylacetylene (11)

A mixture of p-anisaldehyde phenylhydrazone (34b, 4.52 g, 0.02 mol) and DBA (4.68 g, 0.02 mol) in methanol (100 ml) was refluxed for 60 hr, during which period an yellow solid precipitated out. This solid material was filtered off and recrystallized from chloroform to give 1.5 g of an unidentified product (37), mp 238° (d).

Anal. Calcd for $C_{62}H_{44}N_2O_7$: C, 80.19; H, 4.72; N, 3.02; Found: C, 79.93; H, 4.83; N, 3.06.

IR spectrum (KBr) ν_{max}: 3060 and 3020 (ν_{C-H}), 2930 and 2840 (ν_{CH_3}), 1680 and 1660 ($\nu_{C=O}$), 1625 ($\nu_{C=N}$), 1610, 1595 and 1580 ($\nu_{C=C}$), 1515, 1450, 1350, 1180, 1000, 905 and 765 cm^{-1}.

UV spectrum (chloroform) λ_{max}: 258 nm (ε, 33,800), 315 (14,300), 332 (11,900, sh) and 360 (8,400, sh).

NMR spectrum ($CDCl_3$): δ 2.25 (1 H, d, J = 12 Hz), δ 3.10 (1 H, d, J = 12 Hz), δ 3.58 (3 H, s, methoxy), δ 5.16 (1 H, d, J = 6 Hz) and δ 7.25 (38 H, m, aromatic).

^{13}C NMR spectrum ($CDCl_3$): δ 43.56, 55.27, 82.33, 91.17, 103.10, 113.49, 113.89, 120.62, 125.74, 125.98, 127.25, 127.91, 128.15, 128.28, 128.59, 128.65, 128.93, 129.46, 130.11, 130.39, 130.70, 131.04, 131.22, 132.62, 132.84, 132.87, 137.14, 137.55, 137.61, 137.83, 139.81, 143.28, 160.92, 190.81 and 191.27.

5 hr. Subsequent work-up in the usual manner gave a product, which was recrystallized from a mixture (1.1) of benzene and petroleum ether to give 0.4 g (91%) of 3,4-dibenzoyl-5,6-diphenylpyridazine (45), mp 225°.

Anal. Calcd for $C_{30}H_{20}N_2O_2$: C, 81.82; H, 4.54; N, 6.36; Mol. wt., 440. Found: C, 81.40; H, 4.77; N, 6.32; Mol. wt., 440 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3080 and 3045 (ν_{C-H}, aromatic), 1665 ($\nu_{C=O}$), 1590 and 1540 cm^{-1} ($\nu_{C=C}$).

UV spectrum (chloroform) λ_{max}: 270 nm (ε, 25,700).

B In Methanol at Room Temperature

A mixture of 40a (0.224 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was stirred at room temperature for 5 hr, during which period a solid material precipitated, which was subsequently filtered off and recrystallized from benzene at room temperature to give 0.105 g (23%) of 2-(N-(1',2'-diaza-3',4'-diphenyl-4'-oxobut-2'-ene))-1,4-diphenylbut-2-ene-1,4-dione (42), mp 145-146°.

Anal. Calcd for $C_{30}H_{22}N_2O_3$: C, 78.59; H, 4.80; N, 6.11; Found: C, 78.41; H, 4.62; N, 6.01.

IR spectrum (KBr) ν_{max}: 3140 (ν_{N-H}), 3080 (ν_{C-H}, aromatic), 1666 ($\nu_{C=O}$), 1624 ($\nu_{C=N}$), 1606, 1566 and 1546 cm^{-1} ($\nu_{C=C}$).

The mother liquor, obtained after the removal of the solid material (42), was concentrated to give a solid product, which was recrystallized from a mixture (1:1) of benzene and petroleum ether to give 0.3 g (68%) of 3,4-dibenzoyl-5,6-diphenylpyridazine (45), mp 225° (mixture melting point).

II.4.14 Conversion of 2-(N-(1',2'-Diaza-3',4'-diphenyl-4'-oxobut-2'-ene))-1,4-diphenylbut-2-ene-1,4-dione (42) to 3,4-Dibenzoyl-5,6-diphenylpyridazine (45)

A solution of 42 (0.105 g, 0.23 mmol) in benzene (10 ml) was refluxed for ½ hr. Removal of the solvent under vacuum and recrystallization of the product from a mixture (1:1) of benzene and petroleum ether gave 90 mg (88%) of 3,4-dibenzoyl-5,6-diphenylpyridazine (45), mp 225° (mixture melting point).

II.4.15 Reaction of 3,4-Dibenzoyl-5,6-diphenylpyridazine (45) with Hydrazine Hydrate

A mixture of 3,4-dibenzoyl-5,6-diphenypyridazine (45, 0.22 g, 0.5 mmol) and hydrazine hydrate (55 mg, 1 mmol) in ethanol (15 ml) was refluxed for 1 hr. The reaction mixture gave a yellow solid which was filtered off and recrystallized from ethanol to give 0.13 g (68%) of 3,4,5,8-tetraphenylpyridazino[4,5-c]pyridazine (46), mp 234°.

Anal. Calcd for $C_{30}H_{20}N_4$: C, 82.56; H, 4.58; N, 12.84; Mol. wt., 436. Found: C, 83.04; H, 4.28, N, 13.1; Mol. wt., 436 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}, aromatic), 1520, 1480 and 1450 cm^{-1} ($\nu_{C=C}$ and $\nu_{C=N}$).

UV spectrum (chloroform) λ_{max}: 232 nm (ε, 22,000), 300 (10,500) and 330 (8,400).

II.4.16 Attempted Reaction of Benzil Monophenylhydrazone (40b) with Dibenzoylacetylene (11)

A In Methanol Under Refluxing Conditions

A mixture of benzil monophenylhydrazone (40b, 0.3 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was refluxed for 24 hr. Work-up in the usual manner gave 0.27 g (90%) of the unchanged starting material (43b), mp 135° (mixture melting point) and 0.165 g (70%) of DBA, mp 111° (mixture melting point).

B In Tetrahydrofuran Under Refluxing Conditions and in the Presence of Potassium Carbonate

A mixture of 40b (0.3 g, 1 mmol), DBA (0.234 g, 1 mmol) and anhydrous potassium carbonate (0.138 g, 1 mmol) in THF (20 ml) was refluxed for 24 hr. Subsequent work-up, in the usual manner, gave 0.24 g (80%) of 40b, mp 135° (mixture melting point) and 0.175 g (75%) of DBA, mp 111° (mixture melting point).

C In Toluene Under Refluxing Conditions and in the Presence of Potassium Carbonate

A mixture of 40b (0.3 g, 1 mmol), DBA (0.234, 1 mmol) and anhydrous potassium carbonate (0.138 g, 1 mmol) in toluene (20 ml) was refluxed for 36 hr. Work-up in the usual manner gave 0.225 g (75%) of 40b, mp 135° (mixture melting point) and 0.2 g (86%) of DBA, mp 111° (mixture melting point).

D In Xylene Under Refluxing Conditions and in the Presence of Potassium Carbonate

A mixture of 40b (0.3 g, 1 mmol), DBA (0.234 g, 1 mmol) and anhydrous potassium carbonate (0.138 g, 1 mmol) in xylene (20 ml) was refluxed for 12 hr. Subsequent work-up in the usual manner gave 0.27 g (90%) of 40b, mp 135° (mixture melting point) and 0.19 g (80%) of DBA, mp 111° (mixture melting point).

II.4.17 Reaction of Ethylenediamine (47) with Dibenzoylacetylene (11)

A In Methanol at Room Temperature

A mixture of ethylenediamine (47, 60 mg, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was stirred at room temperature for 1 hr, during which period an yellow solid precipitated out. This material was filtered off and recrystallized from a mixture (1:1) of benzene and petroleum ether to

give 85 mg (31%) of N,N'-bis-(2'-(1',4'-diphenylbut-2'-ene-1',4'-dione))-1,2-diaminoethane (52), mp 195-196°.

Anal. Calcd for $C_{34}H_{28}N_2O_4$: C, 77.27; H, 5.11; N, 5.11; Mol. wt., 528. Found: C, 76.77; H, 5.07; N, 5.09; Mol. wt., 528 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3200 (ν_{N-H}, intramolecularly hydrogen-bonded), 3080 (ν_{C-H}, aromatic), 2940 and 2870 (ν_{CH_2}, asymmetric and symmetric), 1680 and 1670 ($\nu_{C=O}$), 1605, 1580 and 1550 cm^{-1} ($\nu_{C=C}$).

UV spectrum (chloroform) λ_{max}: 255 nm (ε, 40,200) and 345 (23,300).

The mother liquor, obtained after the removal of the solid product, was concentrated under reduced pressure to give an orange material, which was recrystallized from methanol to give 0.19 g (69%) of 2-(2'-oxo-2'-phenylethylidene)-3-phenyl-1,2,5,6-tetrahydropyrazine (51), mp 126-127° (lit.[16] mp 120-122°).

Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.27; H, 5.79; N, 10.15; Mol. wt., 276. Found: C, 77.90; H, 5.75; N, 9.80; Mol. wt., 276 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3240 (ν_{N-H}, intramolecularly hydrogen-bonded), 3050 (ν_{C-H}, aromatic), 2920 and 2860 (ν_{CH_2}, asymmetric and symmetric), 1625 ($\nu_{C=O}$, intramolecularly hydrogen-bonded), 1595, 1575 and 1515 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 263 nm (ϵ, 15,800) and 385 (21,100).

B In Tetrahydrofuran at Room Temperature

A mixture of 47 (60 mg, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was stirred at room temperature for 1 hr. Removal of the solvent under vacuum gave an oily mass which was treated with hot methanol (2 ml) to give a yellow solid, which was then recrystallized from a mixture (2:1) of benzene and petroleum ether to give 0.2 g (76%) of N,N'-bis-(2'-(1',4'-diphenyl-but-2'-ene-1',4'-dione))-1,2-diaminoethane (52), mp 195-196° (mixture melting point).

The mother liquor, obtained after the removal of 52, was concentrated under reduced pressure to give 50 mg (18%) of 2-(2'-oxo-2'-phenylethylidene)-3-phenyl-1,2,5,6-tetrahydropyrazine (51), mp 126-127° (mixture melting point).

II.5 REFERENCES

1. For details on the reactions of nucleophiles with acetylenic ketones, see Chapter I of this thesis.

2. N. R. El-Rayyess and F. H. Al-Hajjar, J. Heterocyclic Chem., 14, 367 (1977).

3. F. G. Baddar, F. H. Al-Hajjar and N. R. El-Rayyess, J. Heterocyclic Chem., 15, 385 (1978).

4. Y. A. Al-Farkh, F. H. Al-Hajjar and H. S. Hamoud, Chem. Pharm. Bull., 26, 1298 (1978).

5. L. I. Vereshchagin, E. I. Titova, L. G. Tikhonova, S. R. Buzilova, L. D. Gavrilov and G. A. Kalabin, Zhur. Org. Khim., 10, 978 (1974); Chem. Abstr., 81, 63437 (1974).

6. L. G. Tikhonova, E. I. Titova, L. D. Gavrilov, L. L. Okhapina and L. I. Vereshchagin, Tezisy Dokl.-Vses. Konf. Khim. Atsetilena, 5th, 293 (1975); Chem. Abstr., 89, 24740 (1978).

7. H. W. Heine, T. R. Hoye, P. G. Willard and R. C. Hoye, J. Org. Chem., 38, 2984 (1973).

8. W. Sucrow and M. Slopianka, Chem. Ber., 105, 3807 (1972).

9. V. Bardakos, W. Sucrow and A. Fehlauer, Chem. Ber., 108, 2161 (1975).

10. V. S. Bozdanov, I. L. Mikhelashvili and E. N. Prilezhaeva, Izv. Akad. Nauk SSSR, Ser. Khim., 2374 (1972); Chem. Abstr., 78, 28756 (1973).

11. S. Lahiri, M. P. Mahajan, R. Prasad and M. V. George, Tetrahedron, 33, 3159 (1977).

12. G. Bianchi, A. G. Invernizzi and R. Gandolfi, J. Chem. Soc. Perkin I, 1757 (1974).

13. H. Budzikiewicz, C. Djerassi and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San-Francisco, 1967, p. 643.

14. A. Engelmann and W. Kirmse, Chem. Ber., 106, 3092 (1973).

15. M. J. Haddaddin and R. A. Abi-Rafi, Private Communication.

16. D. H. Hankovszky, K. Hideg and D. Lloyd, J. Chem. Soc. Perkin I, 1619 (1974).

17. T. Curtius and H. Franzen, Chem. Ber., 35, 3239 (1902).

18. F. Just, Chem. Ber., 19, 1201 (1886).

19. C. A. Bischoff, Chem. Ber., 30, 2303 (1897).

20. H. Staudinger and L. Hammet, Helv. Chim. Acta, 4, 217 (1921).

21. H. Staudinger, A. Gaube and J. Siegwart, Helv. Chim. Acta, 4, 212 (1921).

22. E. Fischer, Chem. Ber., 9, 880 (1876).

23. B. M. Lynch and K. H. Pausacker, J. Chem. Soc., 1131 (1954).

24. H. Staudinger and O. Kupfer, Chem. Ber., 44, 2197 (1911).

25. E. Bamberger and J. Grob, Chem. Ber., 34, 523 (1901).

26. R. E. Lutz and W. R. Smithey, J. Org. Chem., 16, 51 (1951).

27. J. B. Conant and R. E. Lutz, J. Am. Chem. Soc., 47, 881 (1925).

CHAPTER III

REACTIONS OF ORTHO-CARBONYL SUBSTITUTED PHENOLS AND ANILINES WITH DIBENZOYLACETYLENE

III.1 ABSTRACT

The reactions of a few ortho-functionalized phenols and anilines with dibenzoylacetylene (DBA, 13) have been examined. The reaction of salicylaldehyde (27a) with DBA, for example, has been shown to give different products, depending on the reaction conditions. Treatment of an equimolar mixture of 27a and DBA in acetone in presence of potassium carbonate at room temperature, for example, gave

a 68% yield of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (30a), whereas in refluxing acetone, under analogous conditions, a 58% yield of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (29a) was obtained. The structures of 30a and 29a have been established on the basis of analytical data, spectral information and chemical evidences. It has been observed that 30a is converted to 29a, in presence of acids or on heating, whereas both 30a and 29a are converted to the same methoxy derivative, 2,3-dibenzoyl-2-methoxy-2H-1-benzopyran (34a), on treatment with concentrated sulfuric acid in methanol. It has been inferred on the basis of UV studies and other supporting evidences that both 30a and 29a are converted to the same benzopyrylium cation 33a, under acidic conditions, which then leads to 34a, in presence of methanol or reverts back to 29a, on reaction with water. Similarly, the reaction of o-hydroxyacetophenone (27b) with DBA has been shown to give a 62% yield of 2,3-dibenzoyl-4-methyl-4H-1-benzopyran-4-ol (30b).

Some of the ortho-carbonyl substituted anilines that we have studied include anthranilamide (35a), anthranilic acid (35b) and ethyl anthranilate (35c). The reaction of 35a-c with DBA gave, in each case, the corresponding 1:1 adducts, namely, 1,4-diphenyl-2-(N-2-carboxamidophenylamino)-but-2-ene-1,4-dione (38a, 89%), 1,4-diphenyl-2-(N-2-carboxyphenylamino)but-2-ene-1,4-dione (38b, 88%) and 1,4-diphenyl-2-(N-2-ethoxycarbonylphenylamino)but-2-ene-1,4-dione

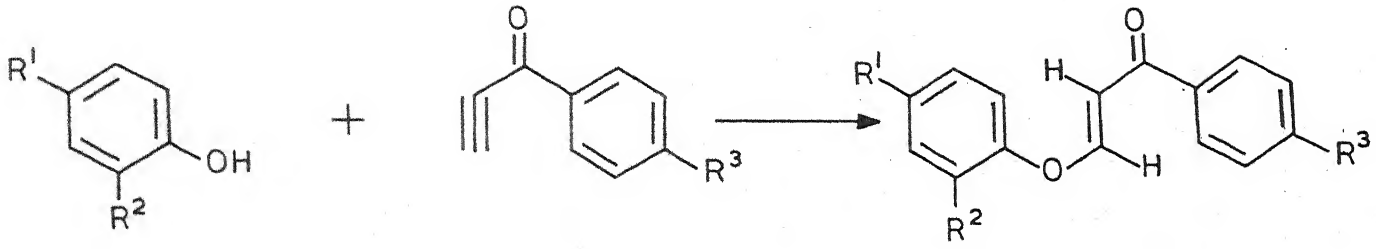
(38c, 70%), respectively. Our attempts to cyclize 38b and 38c under acid catalyzed conditions were unsuccessful and resulted in the formation of cleavage products such as anthranilic acid (35b) and 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (39).

Reasonable mechanisms have been suggested to account for the formation of the various products in these reactions

III.2 INTRODUCTION

Whereas the addition of amines to the activated triple bonds of ethynyl ketones is known to take place readily even at room temperature,[1,2] the nucleophilic additions of alcohols and phenols occur only in the presence of basic catalysts and invariably under more forcing conditions. Thus, it has been shown that phenols react sluggishly with ethynyl ketones even in the presence of catalysts such as sodium phenoxide,[3] pyridine[4] and triethylamine,[5] to give the corresponding 1:1 adducts. Vereshchagin et al.[6] have shown that the branching in acetylenic ketones due to the presence of bulky substituent groups retard the nucleophilic addition of phenols, in an expected manner. In a recent investigation, Venkataramani et al.[7] have shown that phenols (1a-c) add to acetylenic ketones (2a-c) in presence of tricthylamine to give the corresponding enol ethers (3-11) with the trans-stereochemistry, as evidenced by NMR studies (Scheme III.1).

Scheme III.1



1a , $R^1 = R^2 = H$

b , $R^1 = CH_3$; $R^2 = H$

c , $R^1 = H$; $R^2 = NO_2$

2a , $R^3 = H$

b , $R^3 = CH_3$

c , $R^3 = OCH_3$

3 , $R^1 = R^2 = R^3 = H$

4 , $R^1 = R^2 = H$; $R^3 = CH_3$

5 , $R^1 = R^2 = H$; $R^3 = OCH_3$

6 , $R^1 = CH_3$; $R^2 = R^3 = H$

7 , $R^1 = R^3 = CH_3$; $R^2 = H$

8 , $R^1 = CH_3$; $R^2 = H$; $R^3 = OCH_3$

9 , $R^1 = R^3 = H$; $R^2 = NO_2$

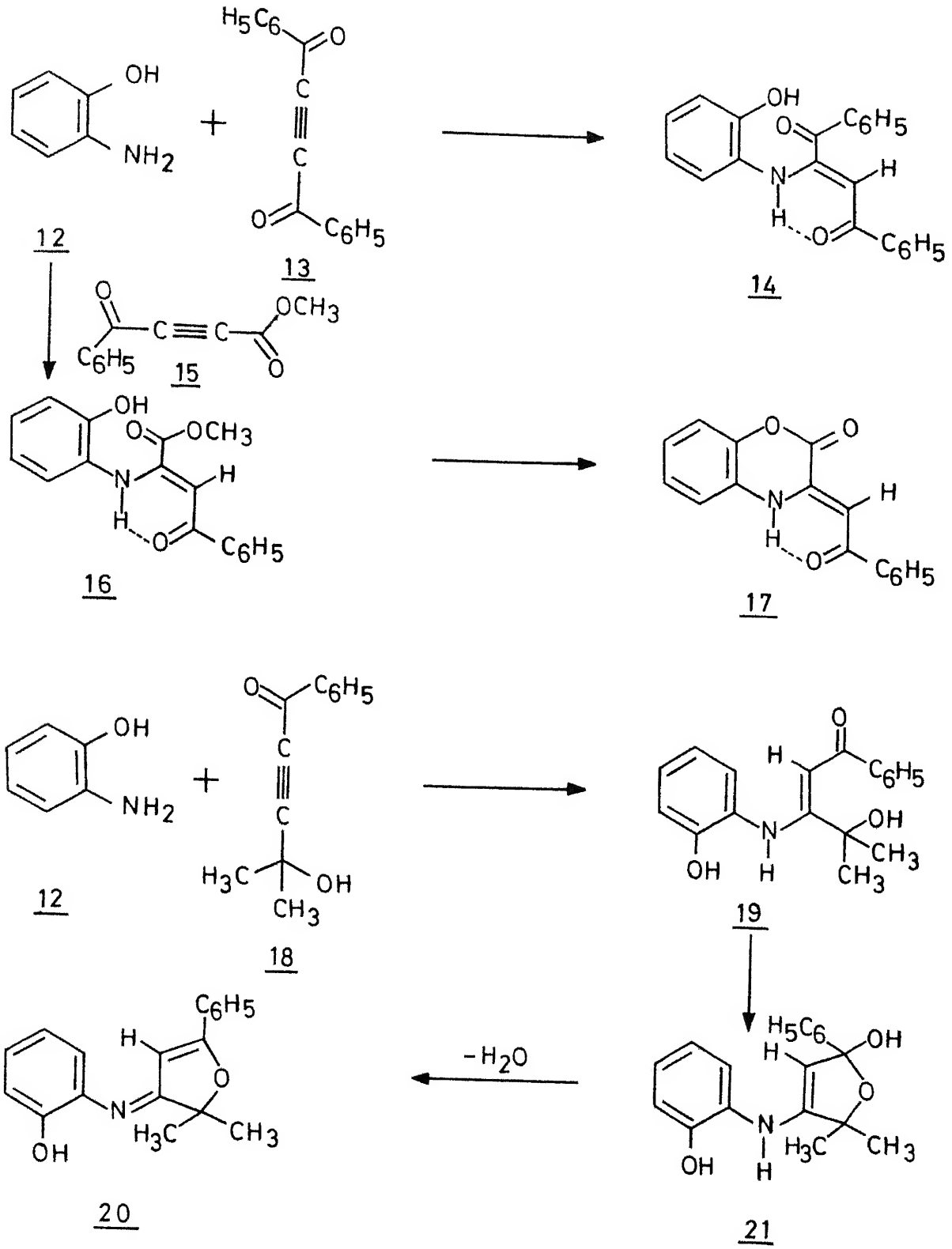
10 , $R^1 = H$; $R^2 = NO_2$; $R^3 = CH_3$

11 , $R^1 = H$; $R^2 = NO_2$; $R^3 = OCH_3$

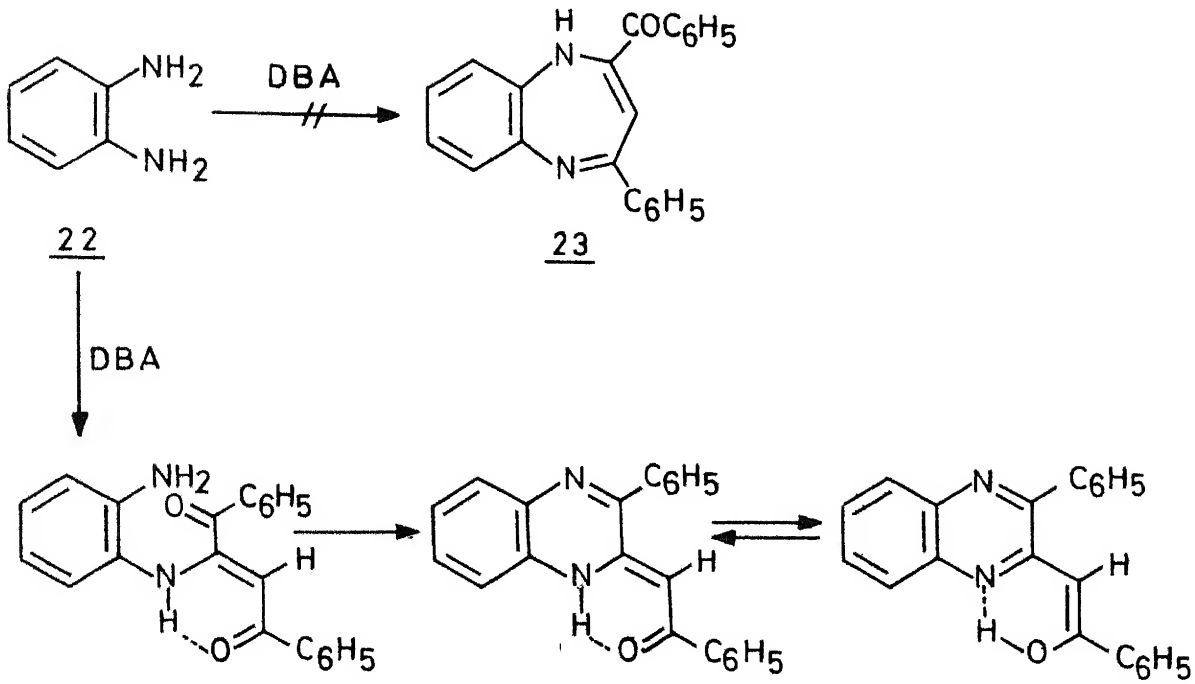
Additions of several ortho-substituted nucleophiles such as o-aminophenol,[8,9] o-phenylenediamine,[9-15] catechol,[16,17] o-hydroxythiophenol[18,19] and o-mercaptothiophenol[20] to acetylenic ketones have been successfully employed for the synthesis of a variety of heterocycles. The reaction of o-aminophenol (12) with DBA (13), for example, has been reported to give 2-(N-2-hydroxyphenylamino)-1,4-diphenylbut-2-ene-1,4-dione (14),[8,9] whereas the reaction of 12 with methyl benzoylpropiolate (15) gives the benzoxazinone, 17[8] (Scheme III.2). The reaction of 12 with 4-hydroxy-4,4-dimethyl-1-phenylbut-2-yn-1-one (18), on the other hand, gives 4-(2-hydroxyphenylimino)-5,5-dimethyl-2-phenyl-4,5-dihydrofuran (20), arising through the loss of elements of water from the initial 1:1 adduct 19, as shown in Scheme III.2.

1H-1,5-Benzodiazepines have been reported to be formed in the reaction of o-phenylenediamine (22) with acetylenic ketones.[10-14] Bindra and LeGoff,[14] for example, have reported that 2-benzoyl-4-phenyl-1H-1,5-benzodiazepine (23) is formed in the reaction of 22 with DBA (Scheme III.3). However, recent studies[9] have shown that the actual product formed in this reaction is 2-(2-hydroxy-2-phenylethenyl)-3-phenylquinoxaline (26), arising through the initially formed 1:1 adduct 24, as shown in Scheme III.3.

Scheme III.2


OH
NH2
H5C6
O
C
C
O
C6H5
12
13
14
15
OCH3
C6H5
16
17
18
19
20
21
H3C
CH3
-H2O

Scheme III 3


NH2
NH2
DBA
H
N
COC6H5
N
C6H5
22
23
DBA
NH2
O
C6H5
N
H
H
O
C6H5
N
C6H5
N
H
H
O
C6H5
N
C6H5
N
H
H
O
C6H5
24
25
26

Quite recently, Potts and Elliott[21] have shown that the reaction of a nucleophile such as o-aminoacetophenone with DBA gives rise to a quinoline derivative, namely, 2,3-dibenzoyl-4-methylquinoline.

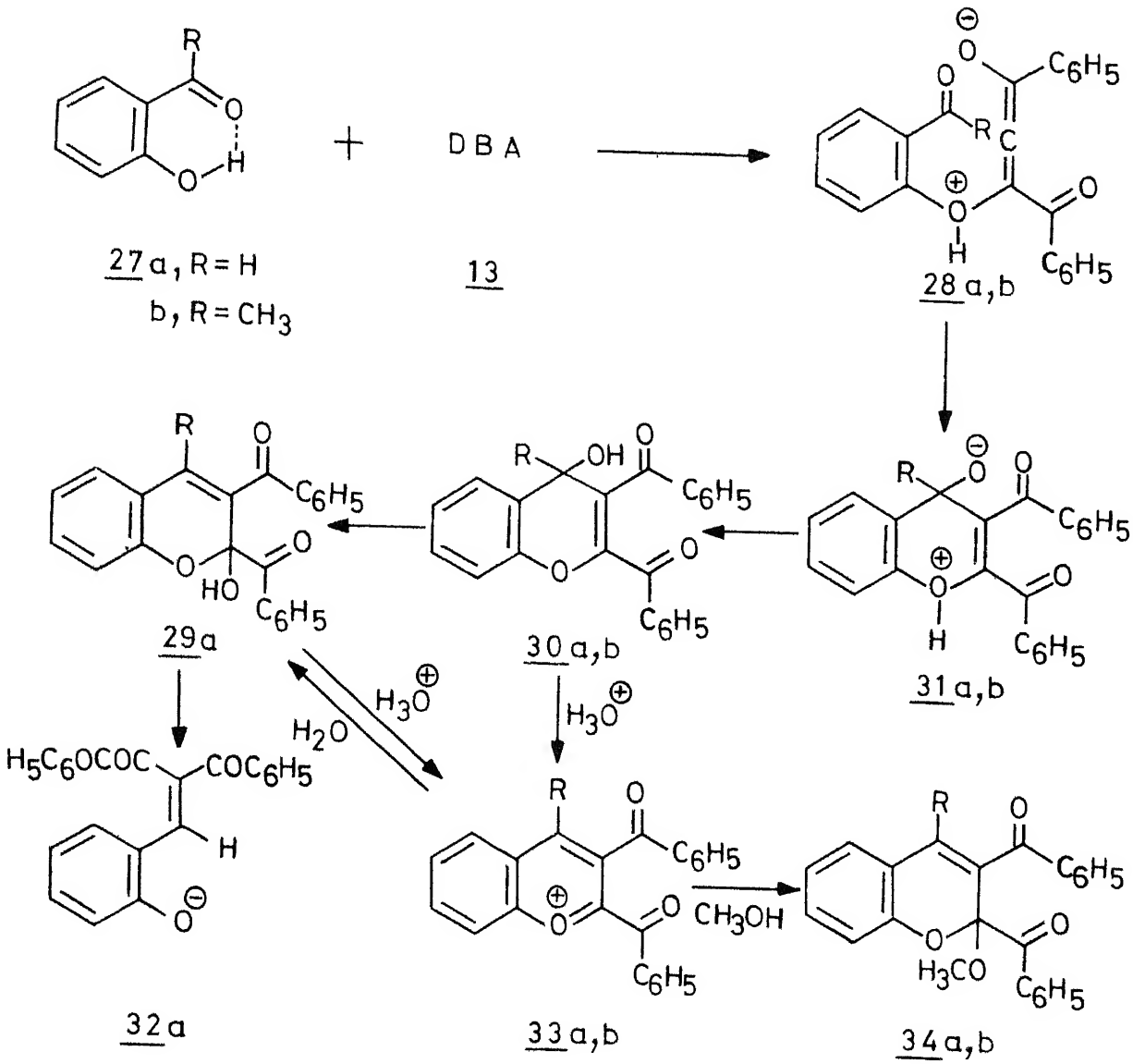
The object of the present investigation has been to examine the reaction of a few ortho-substituted phenols and anilines with DBA, primarily with a view to studying the nature of the products formed in these reactions and also to examine whether these reactions could be used for the synthesis of different heterocycles.

III.3 RESULTS AND DISCUSSION

The ortho-carbonyl substituted phenols that we have employed in the present studies include salicylaldehyde (27a) and o-hydroxyacetophenone (27b). Thus the reaction of 27a with DBA in acetone at room temperature and in the presence of potassium carbonate, gave a 68% yield of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (30a), whereas in refluxing acetone a 58% yield of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (29a) was obtained. (Scheme III.4).

The structures of 30a and 29a have been established on the basis of analytical data, spectral information and chemical evidences. The IR spectrum of 30a, for example, showed a hydroxyl band at 3464 cm^{-1} and two carbonyl absorptions at 1680 and 1660 cm^{-1}, respectively. It has been

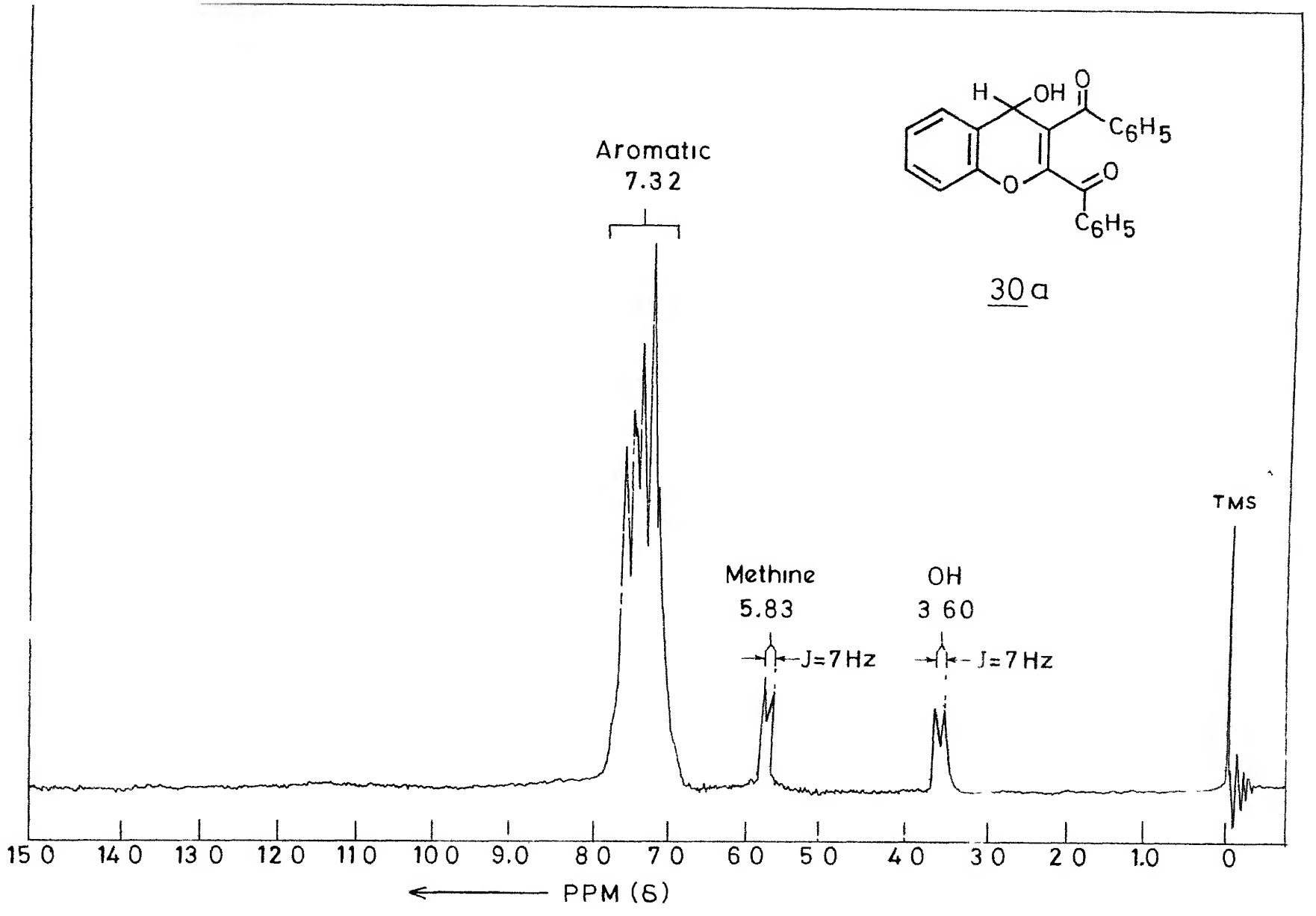
Scheme III 4


R
O
H
O
+
DBA
27a, R = H
b, R = CH3
13
O
C6H5
O
R
C
O
O
H
C6H5
28a,b
R
OH
O
C6H5
O
O
C6H5
30a,b
R
O
O
C6H5
O
H
O
C6H5
31a,b
R
O
O
C6H5
O
HO
C6H5
29a
H3O⊕
H2O
H3O⊕
H5C6OCOC
COC6H5
H
O
32a
R
O
C6H5
O
O
C6H5
33a,b
CH3OH
R
O
C6H5
O
H3CO
C6H5
34a,b

observed that the hydroxyl group in 30a is intramolecularly hydrogen-bonded, as evidenced through concentration dependent IR studies. The NMR spectrum of 30a (Fig. III.1) showed a doublet around δ 3.60 (J = 7 Hz) due to the hydroxyl proton, and a second doublet around δ 5.83 (J = 7 Hz) due to the methine proton. On D_2O-shake, the doublet at δ 3.60 disappeared, whereas the one at δ 5.83 became a singlet, indicating thereby, that the hydroxyl and methine protons are coupled. The aromatic protons (14 H) appeared as a complex multiplet centred around δ 7.32.

The mass spectrum of 30a (Fig. III.2) showed the molecular ion peak at m/e 356 (10). Other peaks were observed at m/e 355 (13), 354 (2), 339 (66), 338 (85), 311 (10), 279 (3), 277 (21), 251 (100), 249 (5), 234 (35), 223 (6), 206 (7), 205 (10), 174 (6), 173 (50), 145 (4), 129 (8), 105 (13), 77 (10) and 51 (10). Some of the possible modes of fragmentation have been shown in Schemes III.5 and III.6.

The UV spectrum of 30a in methanol (Fig. III.3) showed two absorption maxima at 252 nm (ε, 18,800) and 295 (7,500, sh), respectively. The absorption maxima, however, have been shifted to 280 nm (ε, 48,700) and 350 (29,100), respectively, when the spectrum of 30a was determined in concentrated sulfuric acid, indicating thereby, that the benzopyrylium cation 33a is formed under



30 a

Fig. III 1 NMR spectrum (100 MHz) of 30 a.

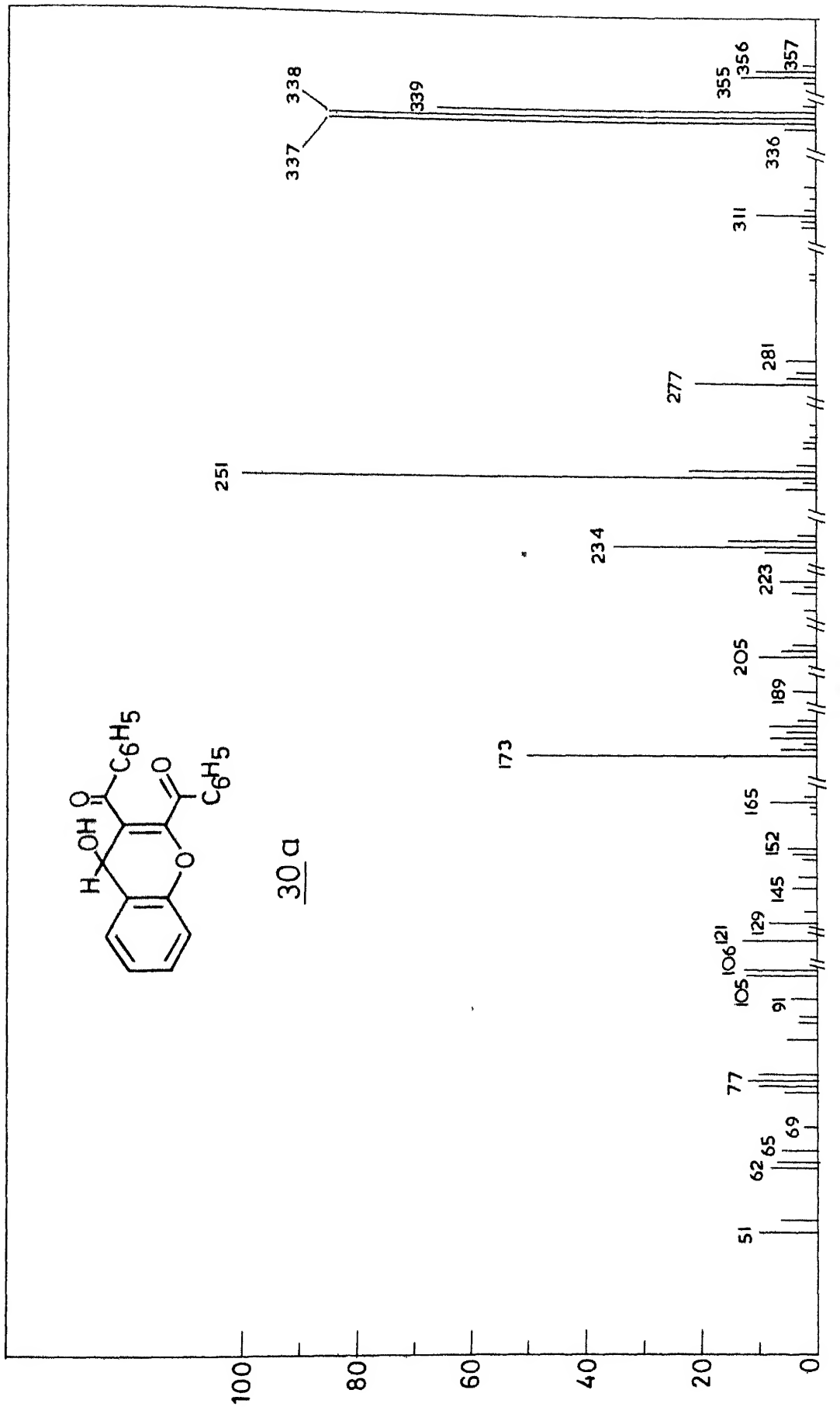
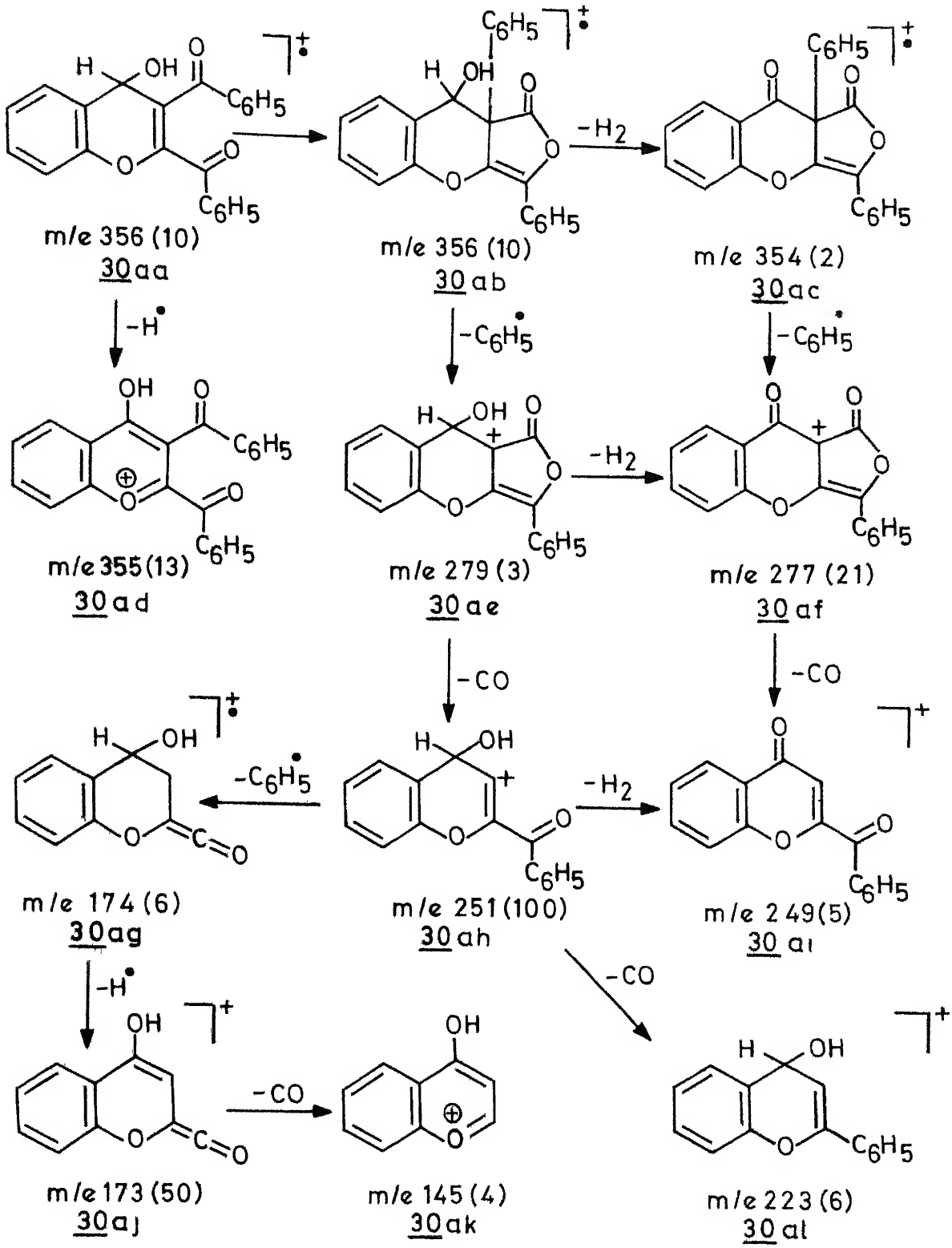
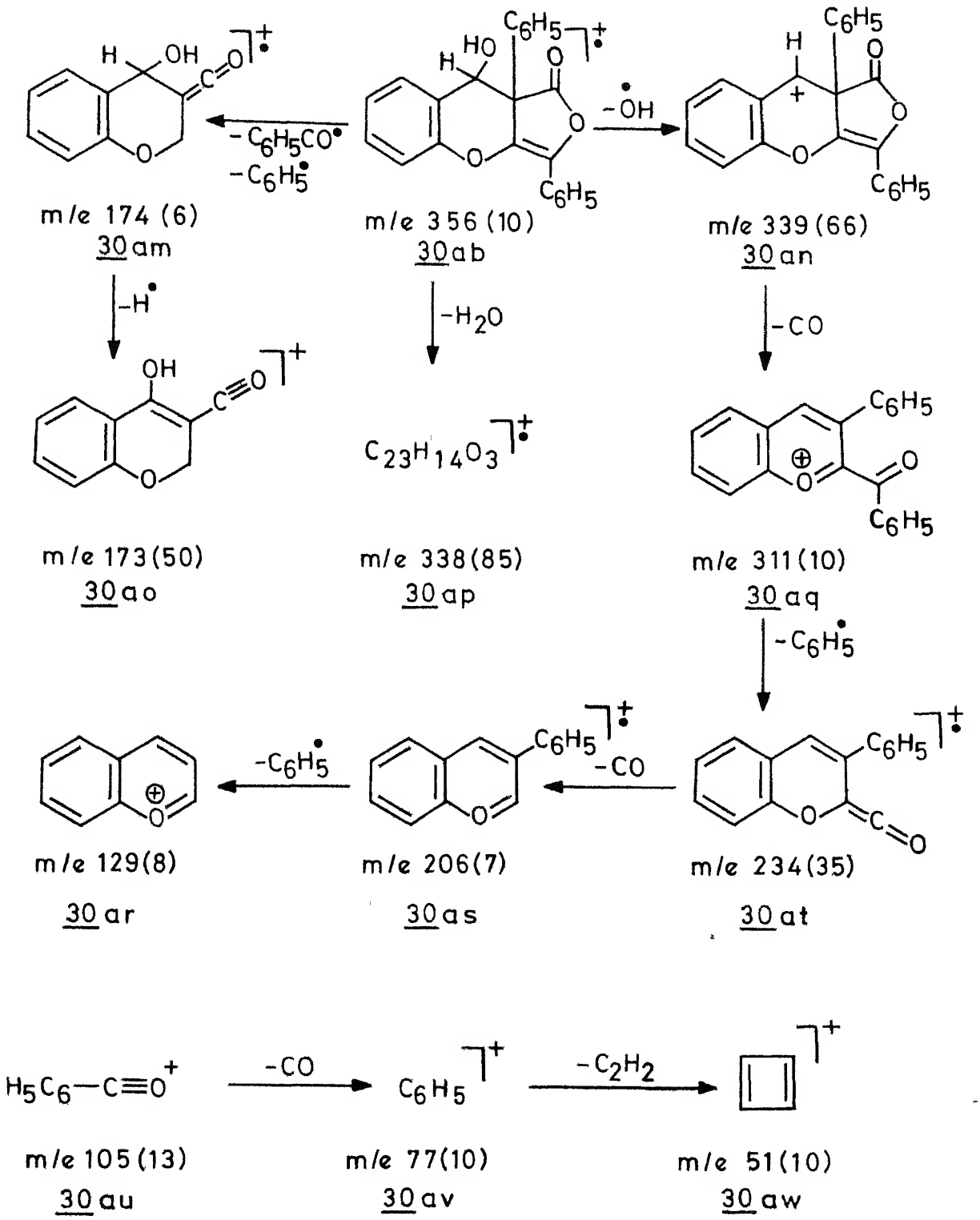


Fig. III.2 Mass spectrum of 30a.

Scheme III 5


m/e 356 (10)
30aa
m/e 356 (10)
30ab
m/e 354 (2)
30ac
m/e 355 (13)
30ad
m/e 279 (3)
30ae
m/e 277 (21)
30af
m/e 174 (6)
30ag
m/e 251 (100)
30ah
m/e 249 (5)
30ai
m/e 173 (50)
30aj
m/e 145 (4)
30ak
m/e 223 (6)
30al

Scheme III.6


m/e 174 (6)
30 am
m/e 356 (10)
30 ab
m/e 339 (66)
30 an
m/e 173 (50)
30 ao
C23H14O3
m/e 338 (85)
30 ap
m/e 311 (10)
30 aq
m/e 129 (8)
30 ar
m/e 206 (7)
30 as
m/e 234 (35)
30 at
m/e 105 (13)
30 au
m/e 77 (10)
30 av
m/e 51 (10)
30 aw

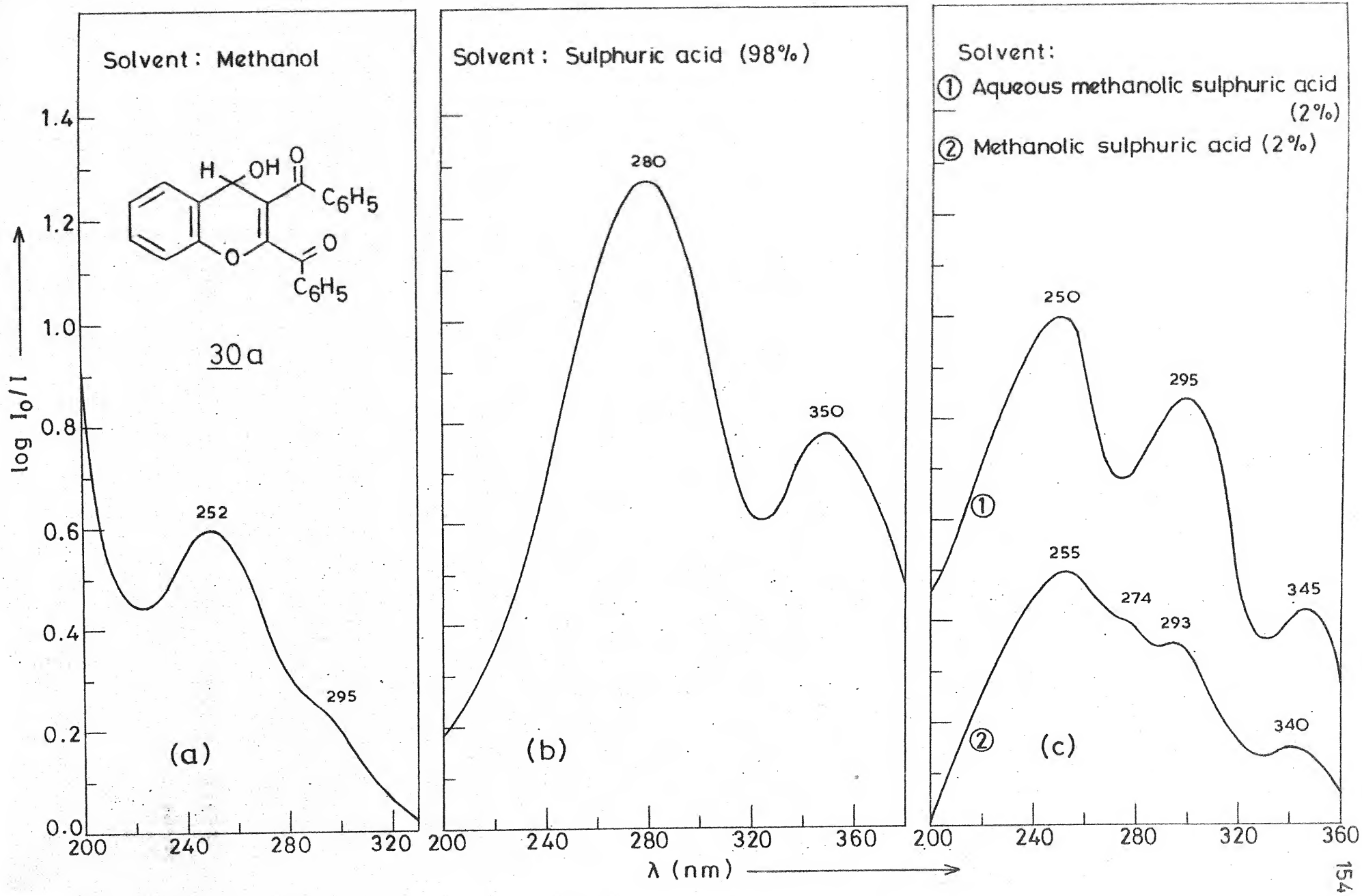


Fig. III.3 UV spectrum of 30a.

these conditions (Scheme III.4). On the other hand, when the spectrum of 30a was recorded in methanolic sulfuric acid, the absorption maxima have been observed at 255 nm (ε, 41,600), 274 (34,100, sh), 293 (30,400) and 340 (12,500), suggesting thereby, that the 2-methoxy-2H-1-benzopyran derivative 34a was formed under these conditions.

The IR spectrum of 29a, likewise, showed a hydroxyl band at 3434 cm^{-1}, whereas the carbonyl absorptions have been observed at 1694 and 1634 cm^{-1}, respectively. The NMR spectrum of 29a (Fig. III.4) showed the hydroxyl proton as a singlet at δ 6.18, which disappeared on D_2O-shake. The complex multiplet centred around δ 7.54 (15 H) has been assigned to the aromatic and vinylic protons.

The UV spectrum of 29a (Fig. III.5) in methanol showed absorption maxima at 245 nm (ε, 23,600), 300 (14,400) and 345 (7,400). The spectrum of 29a in concentrated sulfuric acid (98%), however, showed two absorption maxima at 278 nm (ε, 38,000) and 350 (19,900), characteristic of the benzopyrylium cation 33a. It is interesting to note that the UV spectrum of 29a in a strongly alkaline medium such as methanolic sodium hydroxide (0.7 N), showed absorption maxima at 238 nm (ε, 12,100), 310 (8,300), 332 (12,100) and 460 (4,100), whereas in a weakly alkaline medium (0.001 N sodium hydroxide in methanol), the absorption maxima underwent a hypsochromic

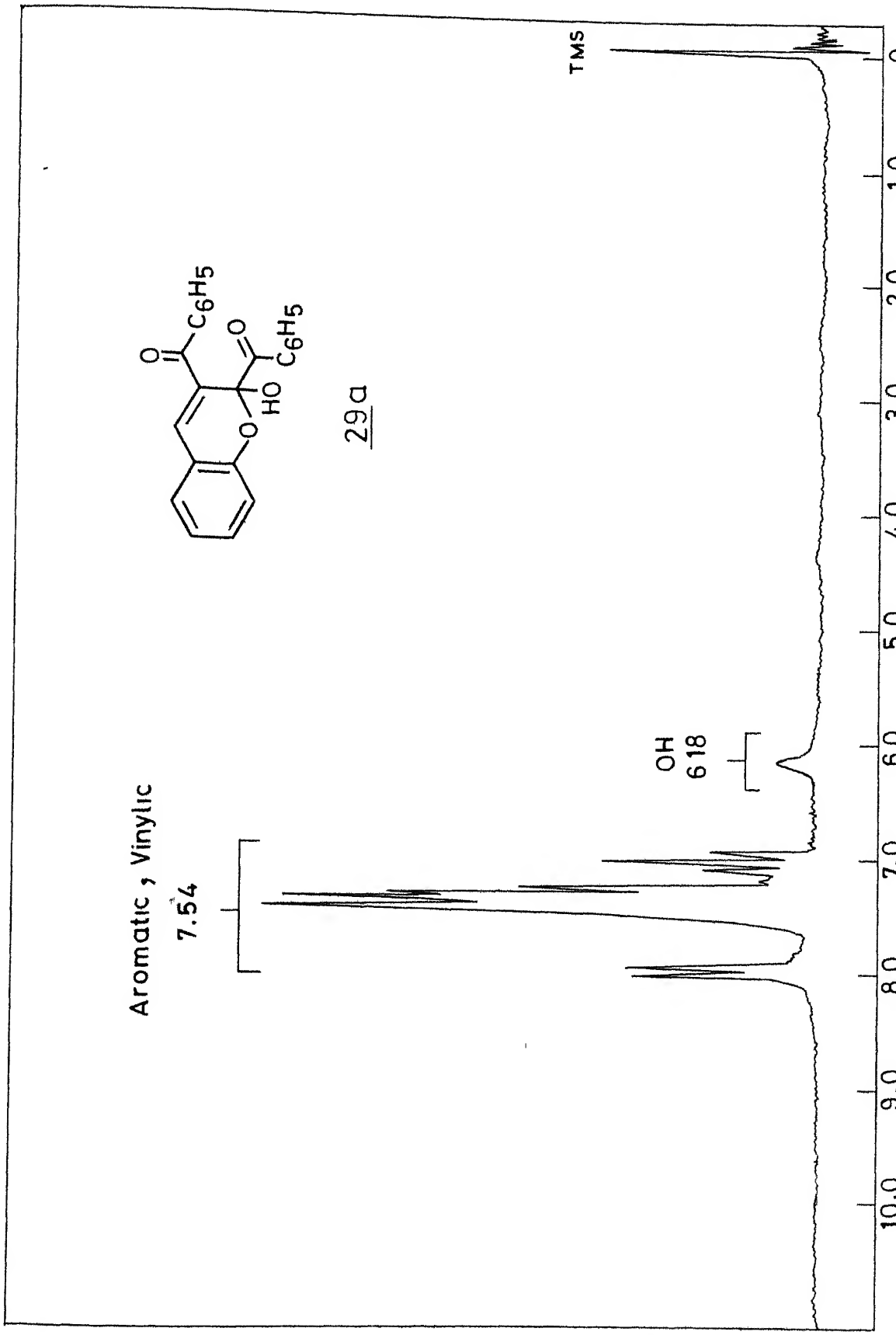


Fig III.4 NMR spectrum (100 MHz) of 29a.

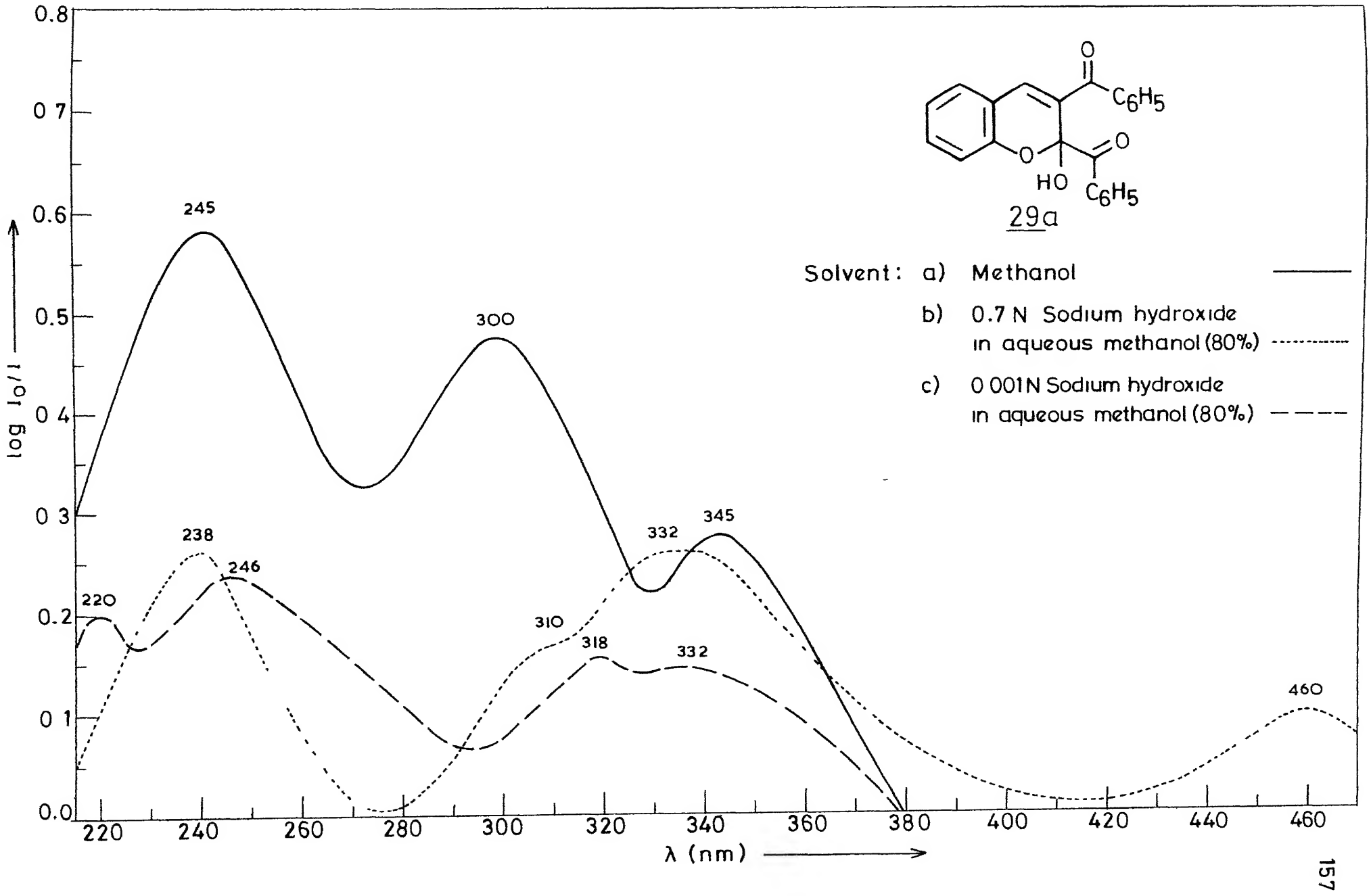


Fig III . 5 UV spectrum of 29a .

shift and were observed at 220 nm (ε, 7,300), 246 (8,100), 318 (5,500) and 332 (5,400). It is reasonable to assume that in a strongly alkaline medium, 29a exists as the ring-opened phenoxide ion 32a, whereas in a weakly alkaline medium, it exists as the phenolic ketone.[22]

The mass spectrum of 29a (Fig. III.6) showed the molecular ion peak at m/e 356 (1). Other peaks were observed at m/e 339 (9), 311 (3), 251 (78), 174 (58), 173 (100), 145 (13), 105 (12), 101 (12), 89 (12), 77 (12) and 51 (11). Some of the probable mass spectral fragmentation patterns have been shown in Scheme III.7.

Further confirmation of the structures of 30a and 29a have been derived through chemical transformations. Refluxing of 30a either in benzene or in methanolic hydrochloric acid gave 29a in yields ranging between 77-80% (Scheme III.4). On the other hand, when 30a in dry methanol was treated with p-toluenesulfonic acid, a 28% yield of 2,3-dibenzoyl-2-methoxy-4H-1-benzopyran (34a) was obtained. Similarly, treatment of 29a in dry methanol with concentrated sulfuric acid gave a 40% yield of 34a.

The structure of 34a, likewise, has been established on the basis of analytical data and spectral evidences. The IR spectrum of 34a, for example, did not show any hydroxyl absorption band, whereas it showed two carbonyl absorption

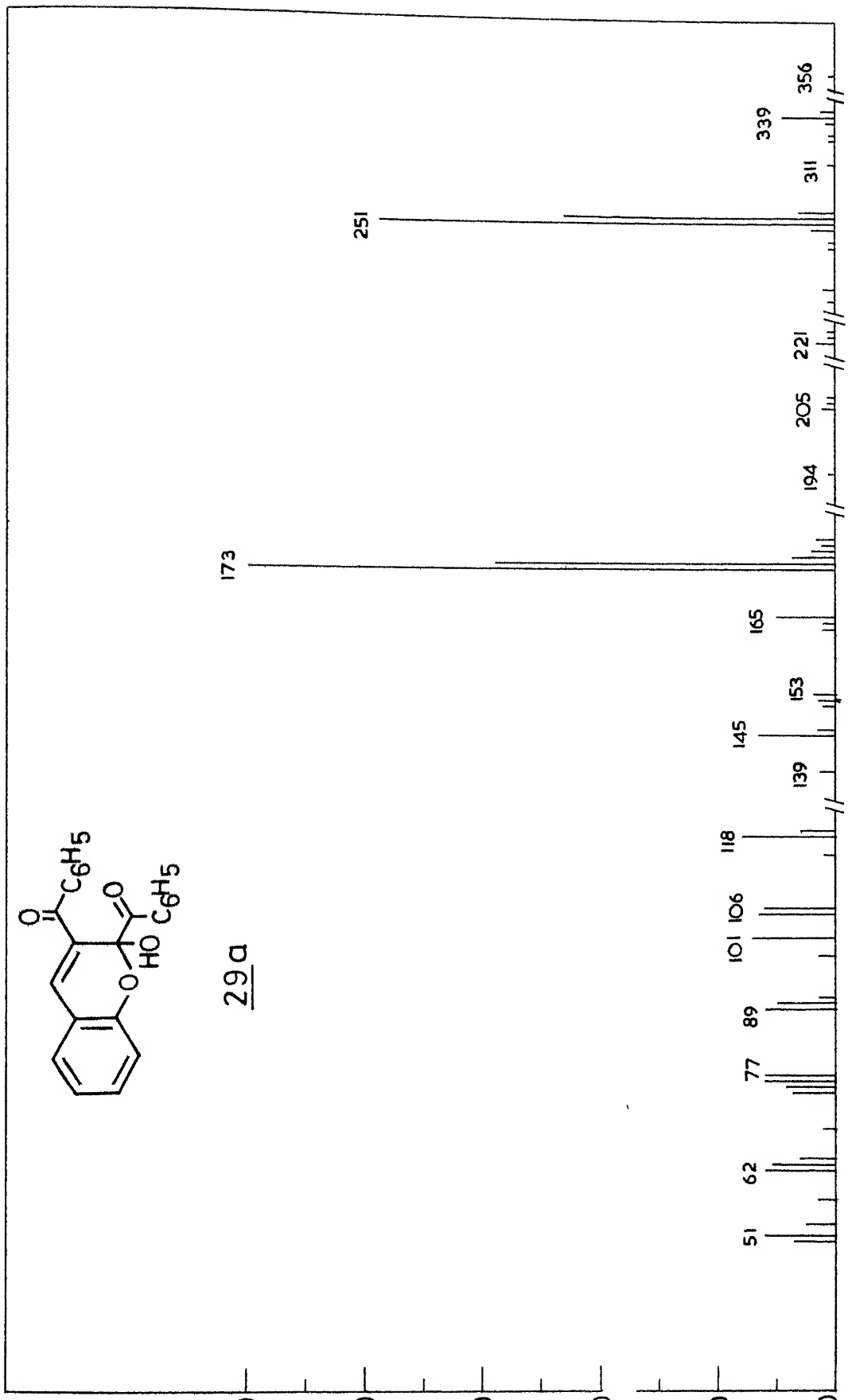
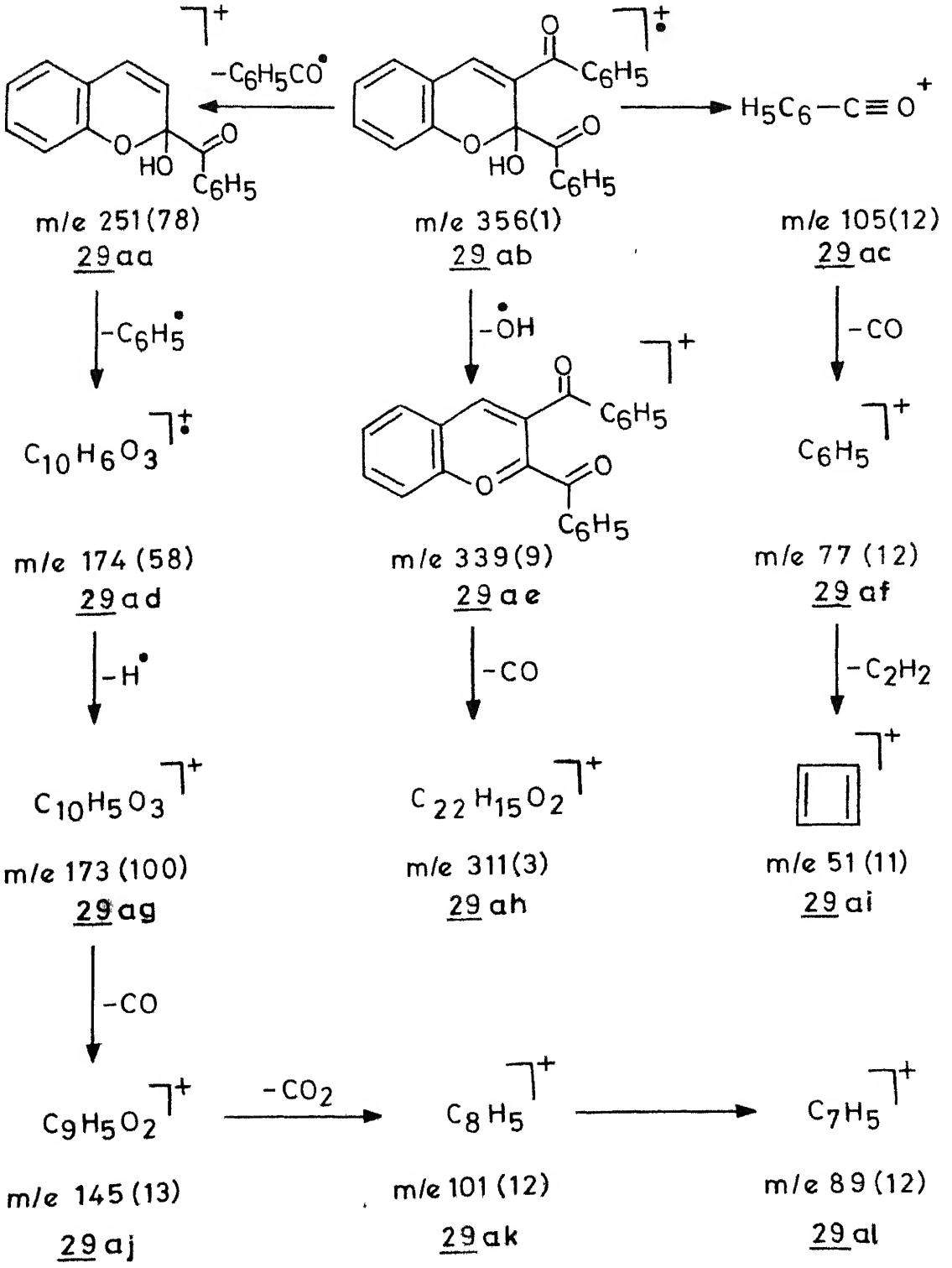


Fig. III.6 Mass spectrum of 29a.

Scheme III.7


-C6H5CO•
m/e 251(78)
29aa
m/e 356(1)
29ab
H5C6—C≡O+
m/e 105(12)
29ac
-C6H5•
-•OH
-CO
C10H6O3
m/e 174 (58)
29ad
m/e 339(9)
29ae
C6H5+
m/e 77 (12)
29af
-H•
-CO
-C2H2
C10H5O3+
m/e 173 (100)
29ag
C22H15O2+
m/e 311(3)
29ah
m/e 51 (11)
29ai
-CO
C9H5O2+
-CO2
C8H5+
C7H5+
m/e 145 (13)
29aj
m/e 101 (12)
29ak
m/e 89 (12)
29al

bands at 1700 and 1650 cm^{-1}, respectively. The NMR spectrum of 34a (Fig. III.7) showed a singlet at δ 3.54 (3 H), assigned to the methoxy protons, whereas the aromatic and vinylic protons appeared as a complex multiplet centred around δ 7.52 (15 H).

The UV spectrum of 34a (Fig. III.8) showed absorption maxima at 245 nm (ε, 38,200), 295 (25,600) and 340 (11,400) and was very much similar to the spectrum of 29a. The UV spectrum of 34a in concentrated sulfuric acid (98%), however, showed absorption maxima at 280 nm (ε, 23,500) and 350 (11,700), characteristic of the benzopyrylium cation (33a) (Scheme III.4).

In continuation of our studies, we have examined the reaction of o-hydroxyacetophenone (27b) with DBA. Treatment of 27b with DBA in acetone at room temperature and in the presence of potassium carbonate gave a 62% yield of 2,3-dibenzoyl-4-methyl-4H-1-benzopyran-4-ol (30b). The IR spectrum of 30b showed two absorption bands at 3560 and 3440 cm^{-1}, which can be assigned to the free and hydrogen-bonded hydroxyl groups. In addition, the spectrum showed two carbonyl absorptions at 1665 and 1630 cm^{-1}, respectively. The NMR spectrum of 30b (Fig. III.9) showed a singlet at δ 1.80 (3 H), assigned to the methyl protons and a second singlet at δ 3.92 (1 H), which disappeared on D_2O-shake and was assigned to the hydroxyl proton. The complex multiplet centred around

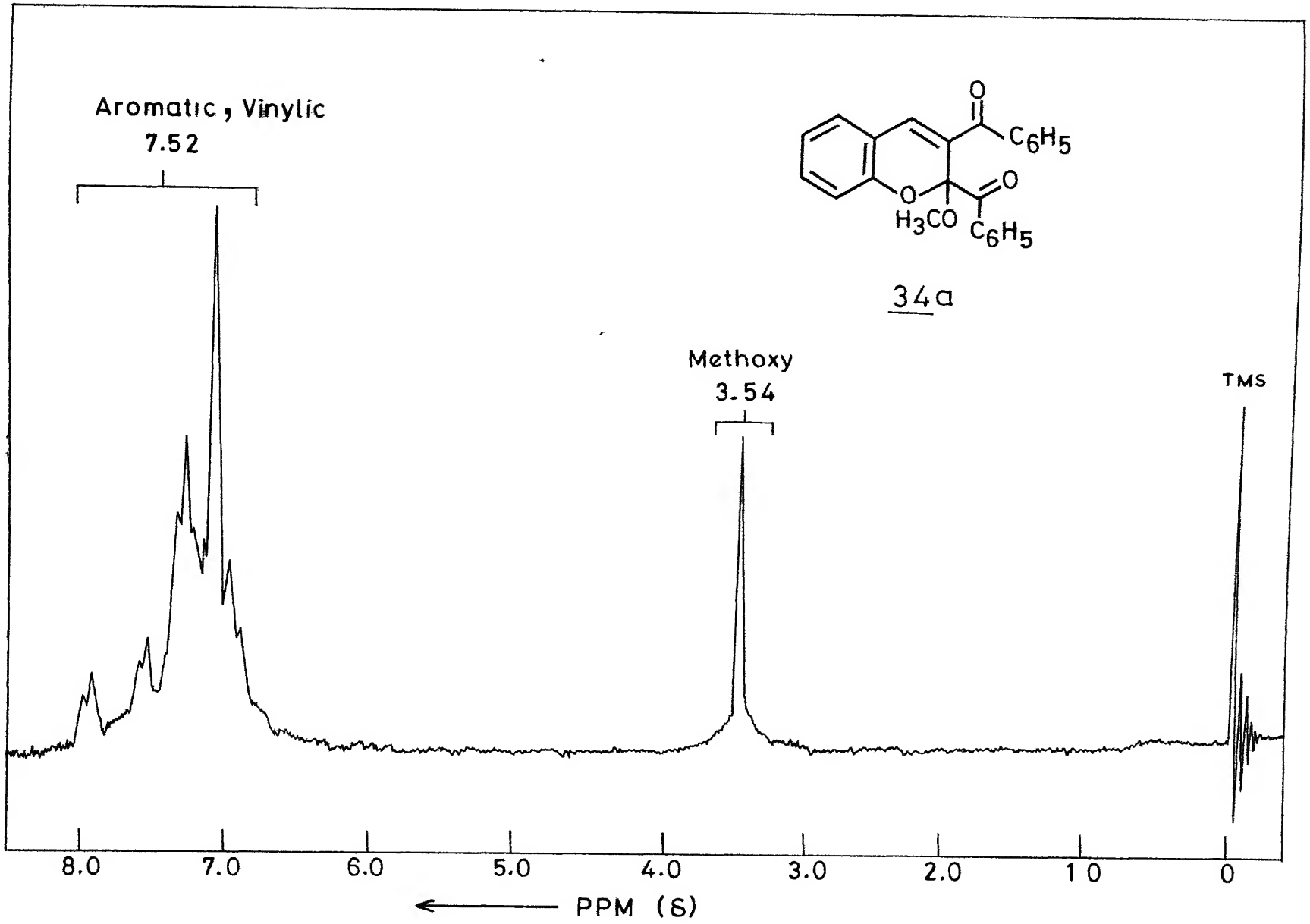


Fig. III.7 NMR spectrum (100 MHz) of 34a .

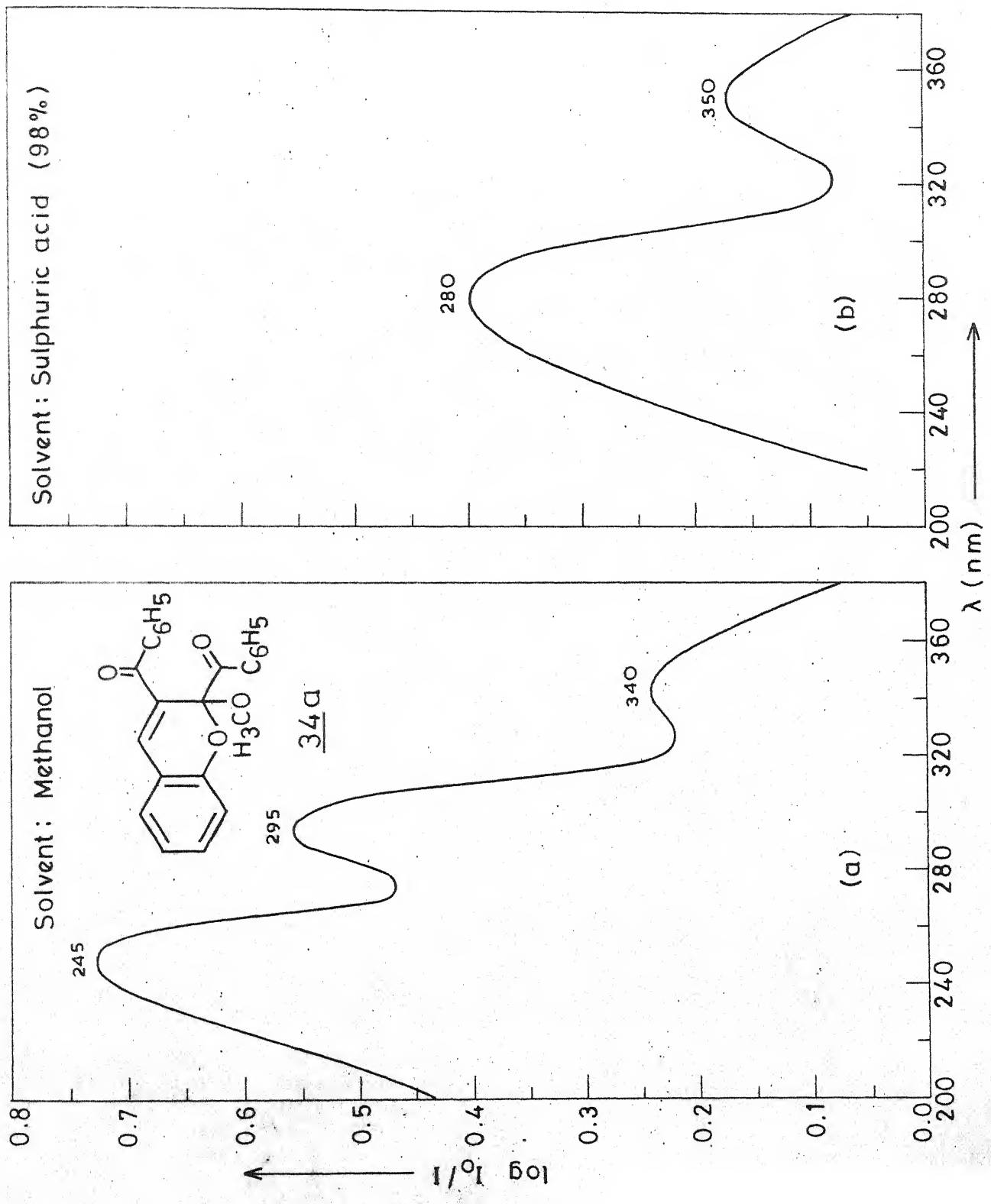


Fig. III . 8 UV spectrum of 34a.

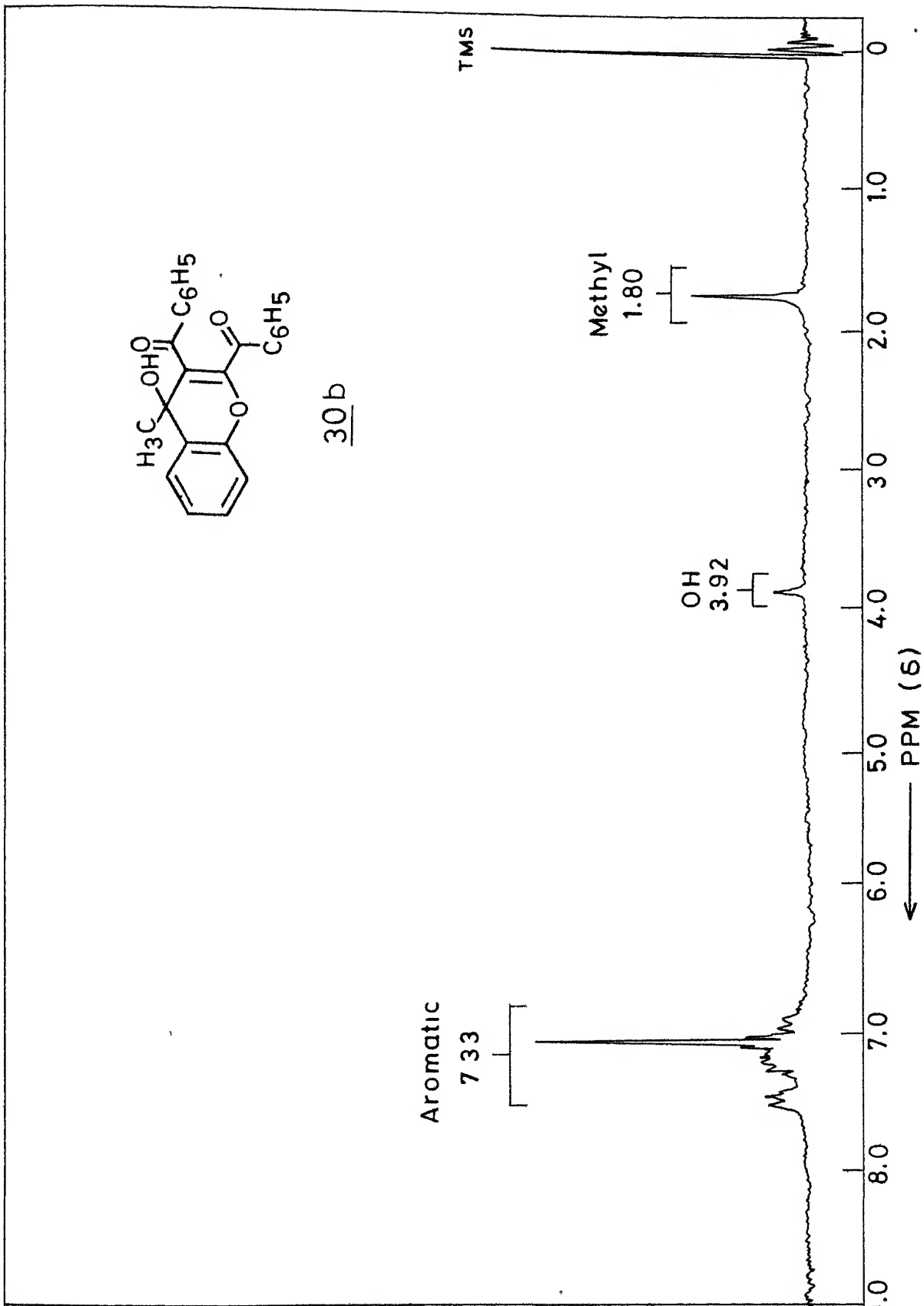


Fig. III 9 NMR spectrum (100 MHz) of 30 b

δ 7.33 (14 H) has been assigned to the aromatic protons. The UV spectrum of 30b in methanol (Fig. III.10) showed absorption maxima at 255 nm (ε, 21,300) and 290 (7,400, sh). The spectrum of 30b in concentrated sulfuric acid, however, showed absorption maxima at 277 nm (ε, 30,900), and 345 (17,700), characteristic of the benzopyrylium cation 33b.

Further confirmation of the structure of 30b has been derived from its mass spectrum (Fig. III.11). The molecular ion peak was observed at m/e 370 (2), whereas other major peaks in the spectrum were observed at m/e 355 (100), 354 (8), 352 (34), 327 (9), 277 (74), 265 (10), 249 (11), 247 (8), 233 (3), 219 (9), 189 (11), 105 (19), 77 (19) and 51 (19). Some of the probable fragmentation patterns are shown in Scheme III.8.

The formation of various products such as 30a, 29a, 30b and 34a in the reaction of salicylaldehyde (27a) and o-hydroxyacetophenone (27b) with DBA has been rationalized in terms of the pathway shown in Scheme III.4. It has been assumed that the nucleophilic addition of 27a,b gives initially the zwitterionic intermediates 28a,b, which then undergo cyclization to give 30a,b. The 4H-1-benzopyran-4-ols 30a,b, would be expected to give the pyrylium cations 33a,b in presence of acids, which in turn can undergo further transformation to give the 2H-1-benzopyran-2-ol, 29a, on reaction

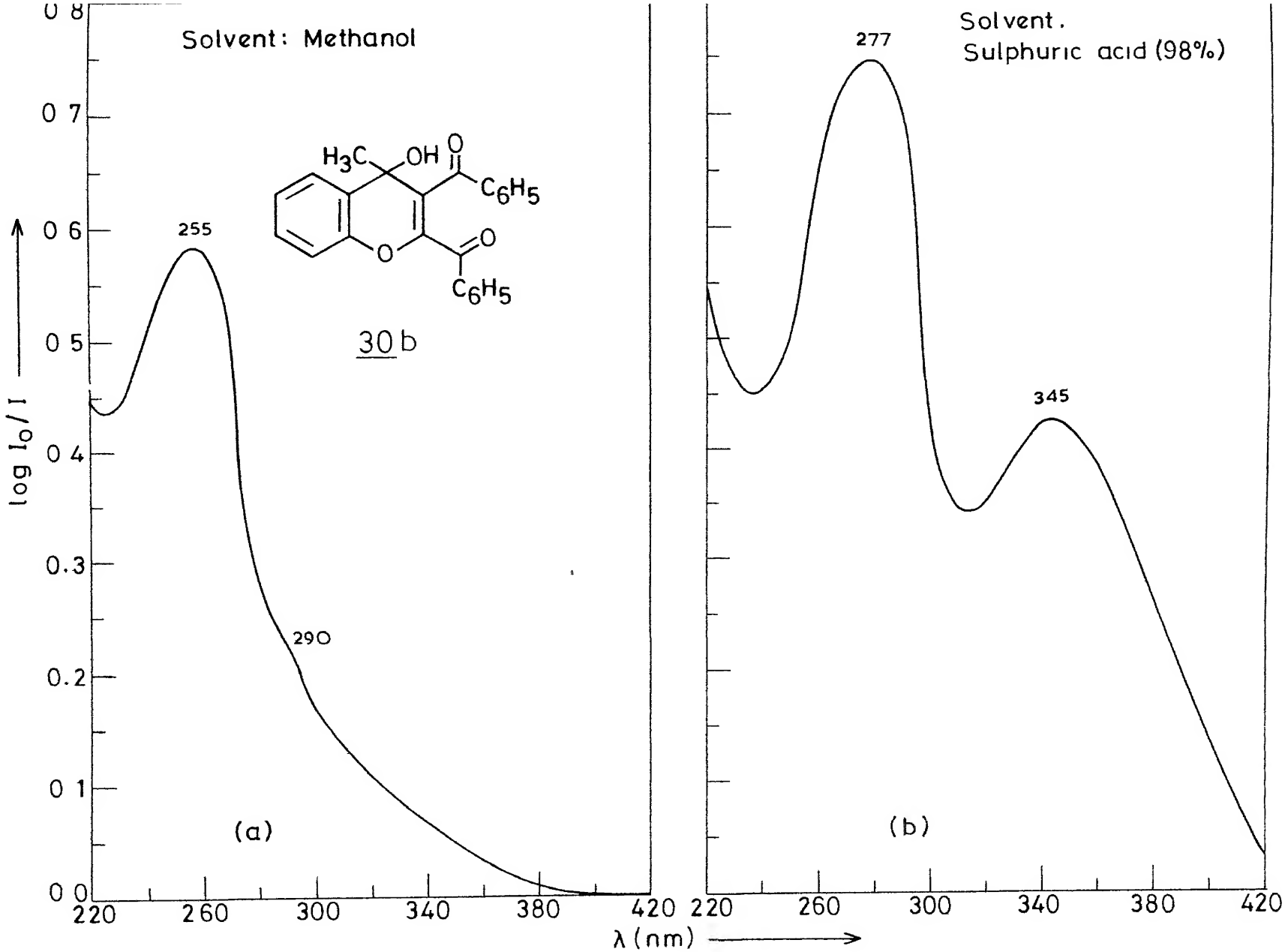


Fig III . 10 UV spectrum of 30 b

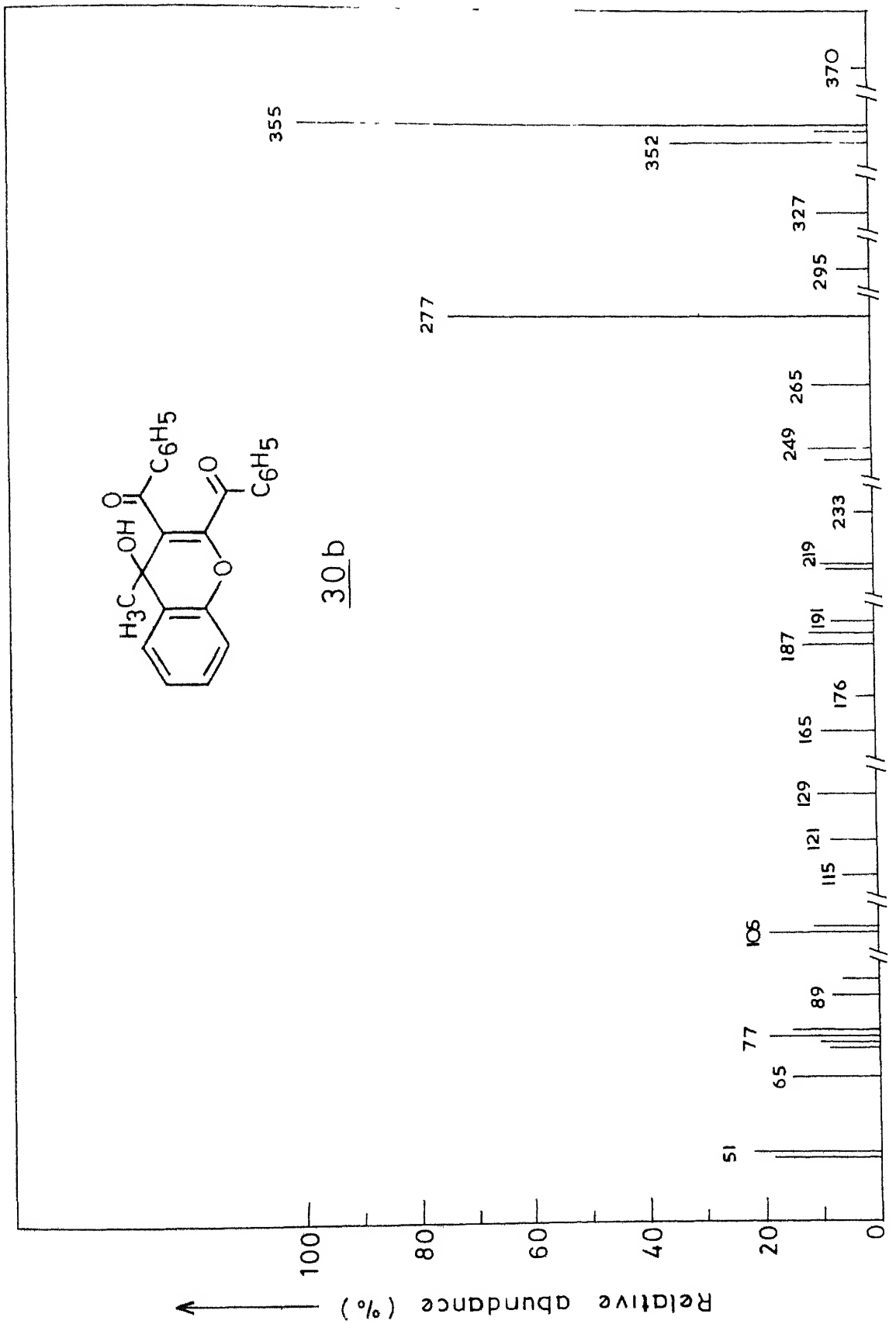
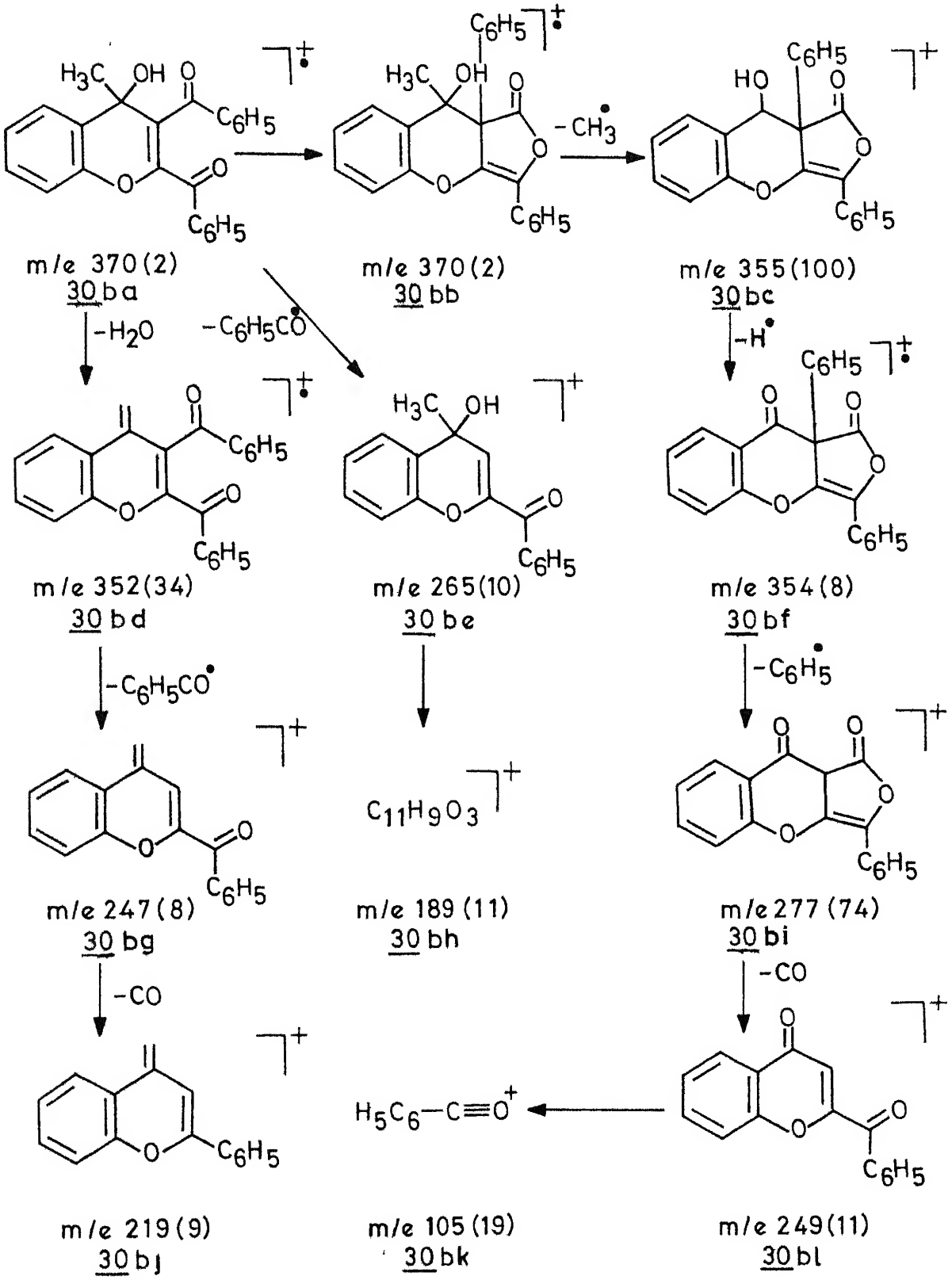


Fig. III.11 Mass spectrum of 30b.

Scheme III . 8

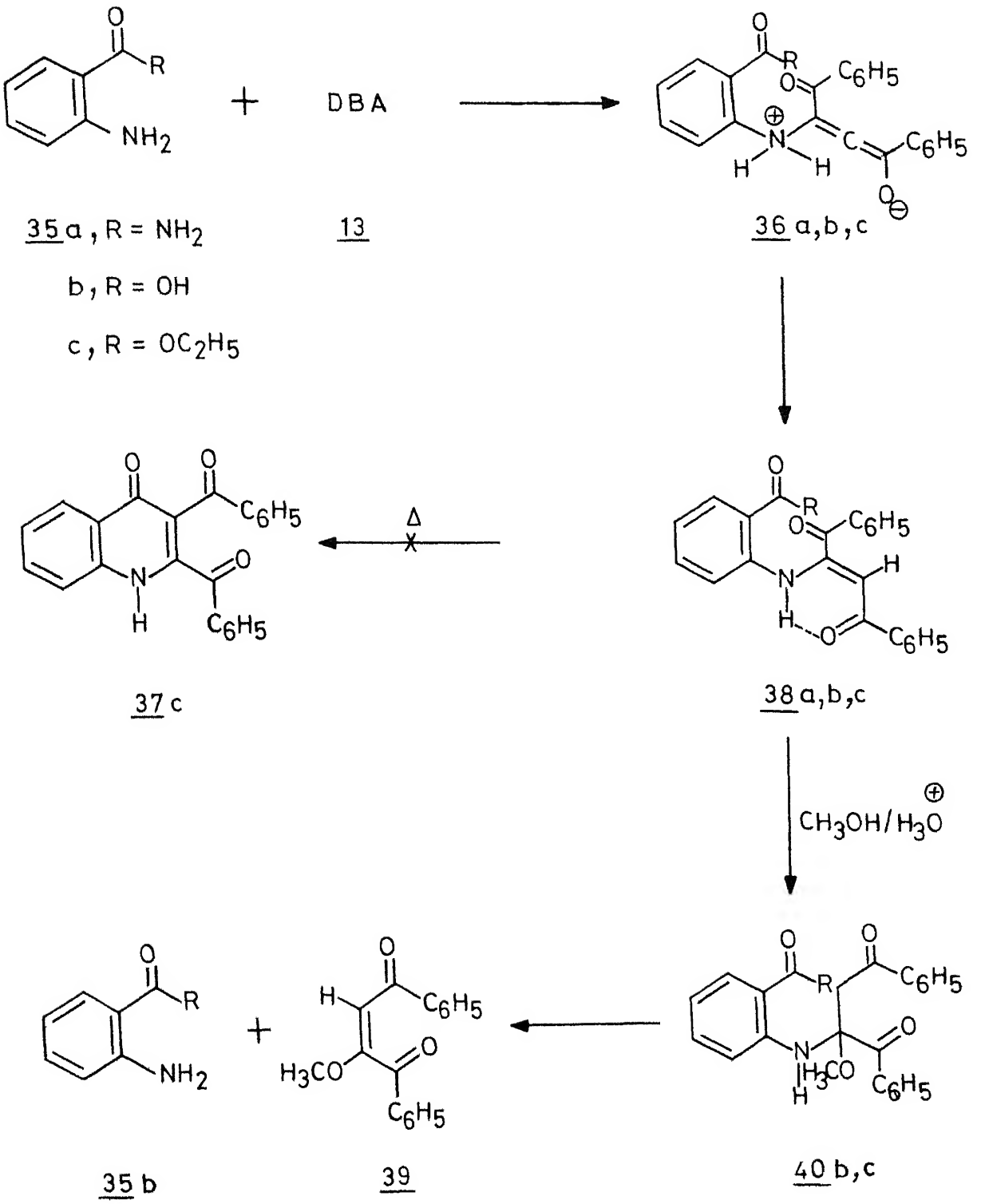

m/e 370 (2)
30 ba
-H2O
-C6H5CO
m/e 370 (2)
30 bb
-CH3
m/e 355 (100)
30 bc
-H
m/e 352 (34)
30 bd
m/e 265 (10)
30 be
m/e 354 (8)
30 bf
-C6H5CO
C11H9O3
-C6H5
m/e 247 (8)
30 bg
m/e 189 (11)
30 bh
m/e 277 (74)
30 bi
-CO
-CO
H5C6-C≡O+
m/e 219 (9)
30 bj
m/e 105 (19)
30 bk
m/e 249 (11)
30 bl

with water. In the presence of dry methanol, however, the benzopyrylium cation 33a, for example, would be expected to give the methoxy derivative 34a. In the presence of alkali, the 2H-1-benzopyran-2-ol, 29a would open up to give the phenoxide anion 32a or the corresponding phenol, as evidenced by UV studies.

In contrast to the reactions of salicylaldehyde and o-hydroxyacetophenone with DBA, the reaction of nucleophiles such as anthranilamide (35a), anthranilic acid (35b) and ethyl anthranilate (35c), gave the corresponding 1:1 adducts, namely, 1,4-diphenyl-2-(N-carboxamidophenylamino)but-2-ene-1,4-dione (38a), 1,4-diphenyl-2-(N-2-carboxyphenylamino)but-2-ene-1,4-dione (38b) and 1,4-diphenyl-2-(N-2-ethoxycarbonylphenylamino)but-2-ene-1,4-dione (38c) in yields ranging between 70-90% (Scheme III.9).

The structures of 38a-c have been established on the basis of analytical results, spectraldata and chemical evidences. The IR spectrum of 38a, for example, showed the asymmetric and symmetric stretching bands of the amide functionality at 3440 and 3320 cm^{-1}, respectively.[23] The intramolecularly hydrogen-bonded, NH band was observed at 3200 cm^{-1}, whereas the carbonyl absorptions were observed at 1670 and 1640 cm^{-1}, respectively. The NMR spectrum of 38a (Fig. III.12) showed a singlet at δ 6.16 (1 H), assigned to the vinylic proton and a second singlet at δ 13.68 (1 H), which disappeared on D_2O-shake,

Scheme III.9


DBA
35 a, R = NH2
b, R = OH
c, R = OC2H5
13
36 a,b,c
38 a,b,c
37 c
Δ
CH3OH/H3O⊕
40 b,c
35 b
39

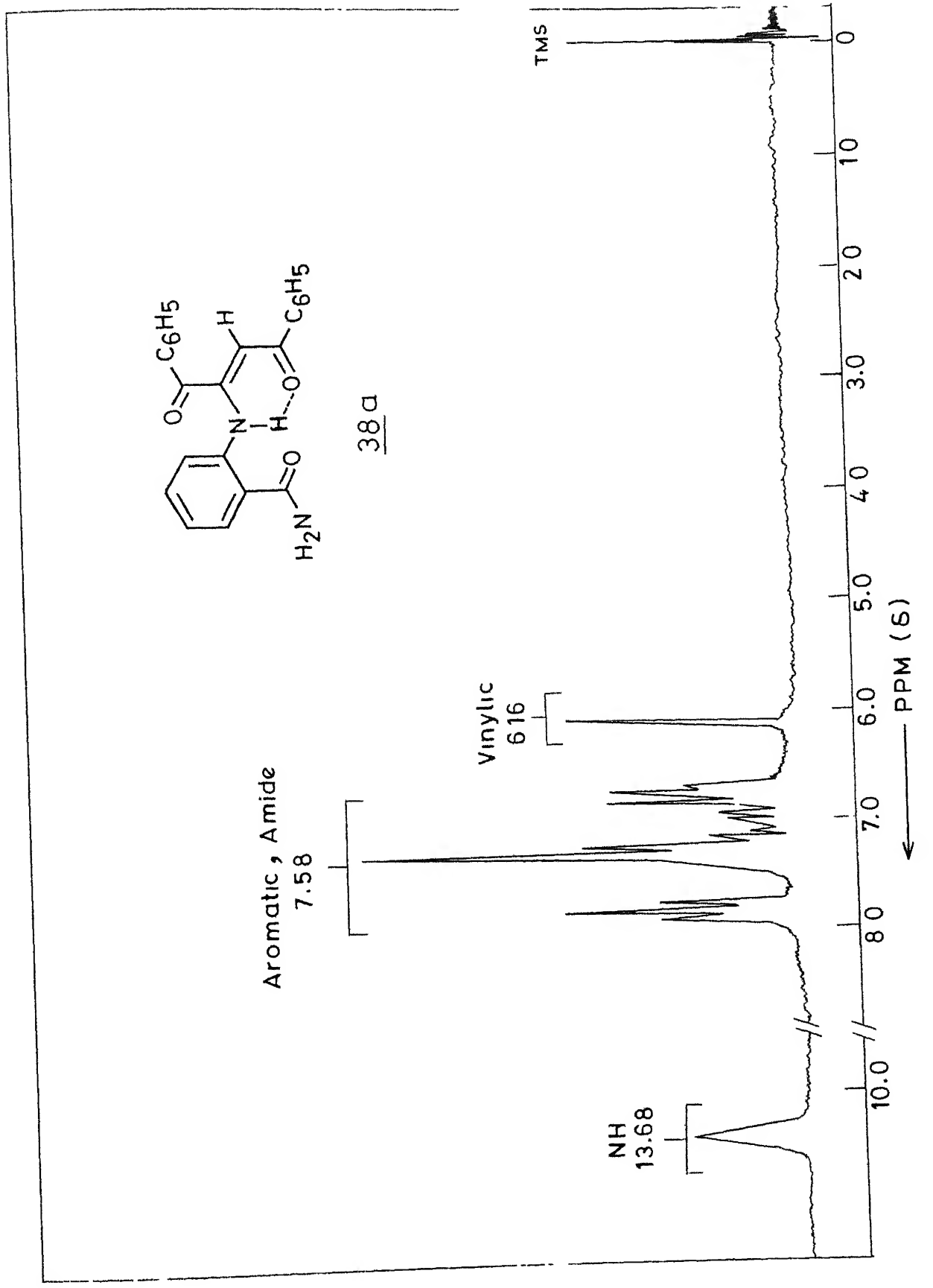


Fig. III .12 NMR spectrum (100 MHz) of 38a

assigned to the hydrogen-bonded NH. The aromatic protons and the amide NH_2 protons appeared as a complex multiplet centred around δ 7.58 (16 H), the amide protons of this multiplet could be exchanged on D_2O-shake. The mass spectrum of 38 (Fig. III.13) showed a molecular ion peak at m/e 370 (2). Other major peaks in the spectrum were observed at m/e 279 (10), 265 (40), 252 (4), 251 (12), 223 (6), 185 (6), 183 (8), 167 (36), 149 (100), 132 (4), 130 (12), 105 (24), 77 (36) and 51 (40). A probable fragmentation mode, which would account for the formation of the various fragments under electron impact, is shown in Scheme III.10.

The IR spectrum of 1,4-diphenyl-2-(N-2-carboxyphenylamino)but-2-ene-1,4-dione (38b) showed a broad band between 2500 and 3200 cm^{-1}, which would account for OH and NH absorptions. The carbonyl absorptions have been observed at 1680 and 1660 cm^{-1}, respectively. The NMR spectrum of 38b (Fig. III.14), showed a singlet at δ 6.30 (1 H), assigned to the vinylic proton and a complex multiplet centred around δ 7.55 (14 H), which could be assigned to the aromatic protons. In addition, the spectrum showed a broad singlet at δ 8.80 (1 H) and a sharp singlet at δ 9.82 (1 H), which were exchangeable with D_2O and have been assigned to the OH of carboxylic acid and the intramolecularly hydrogen-bonded, NH proton, respectively. It might be mentioned in this connection that the NMR assignments of 38b are in agreement with the literature data for analogous substances.[24]

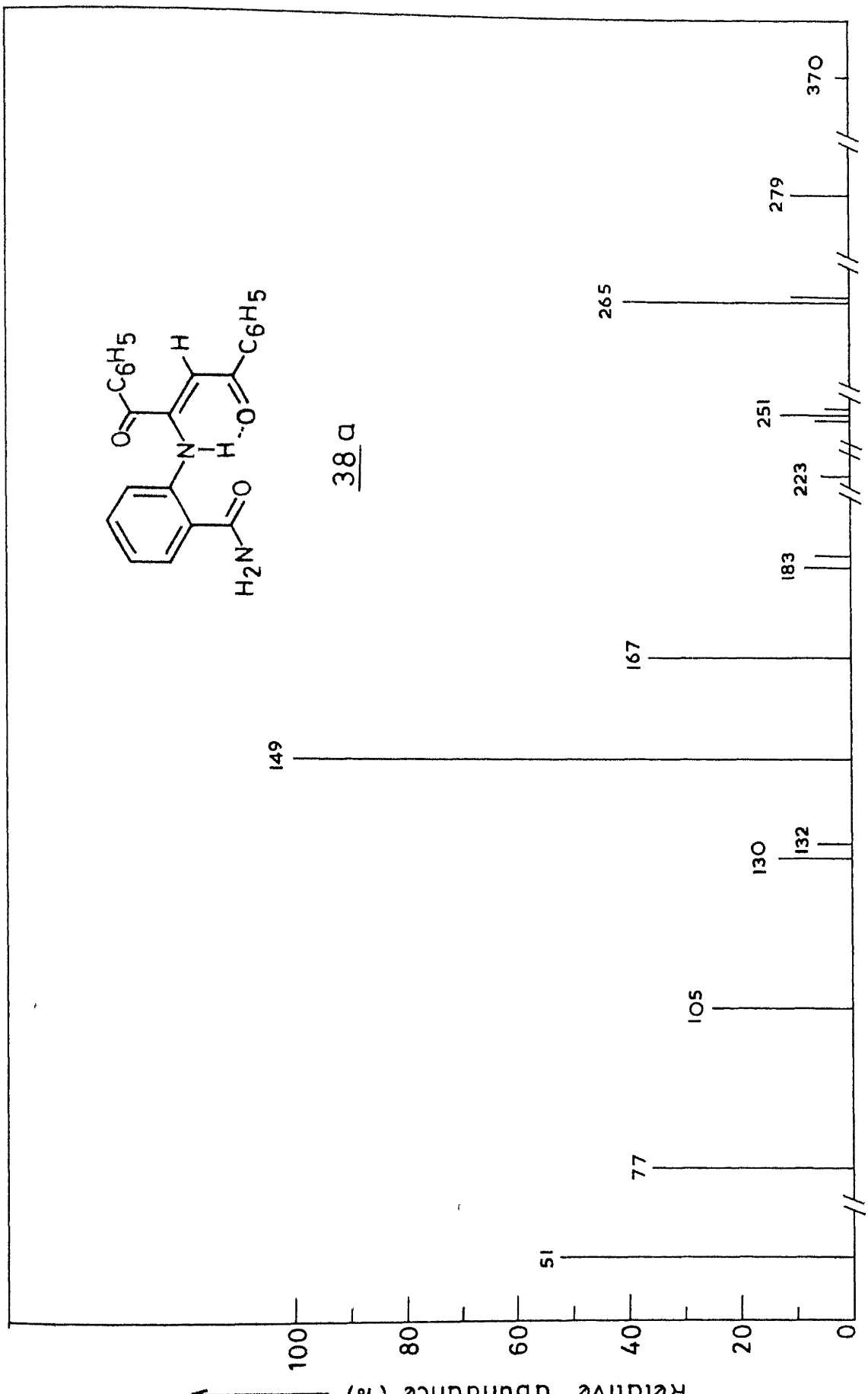
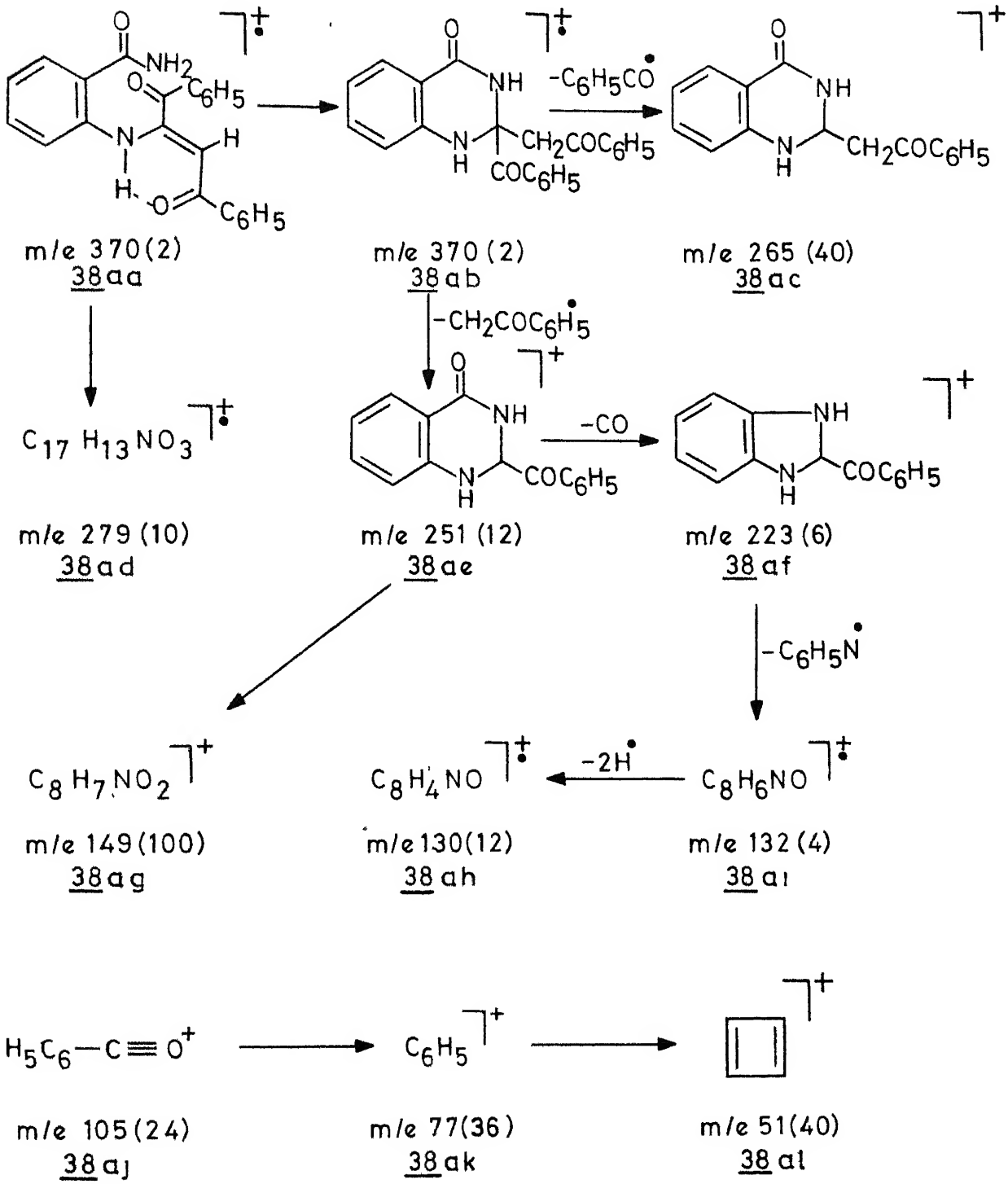


Fig. III.13 Mass spectrum of 38a.

Scheme III .10



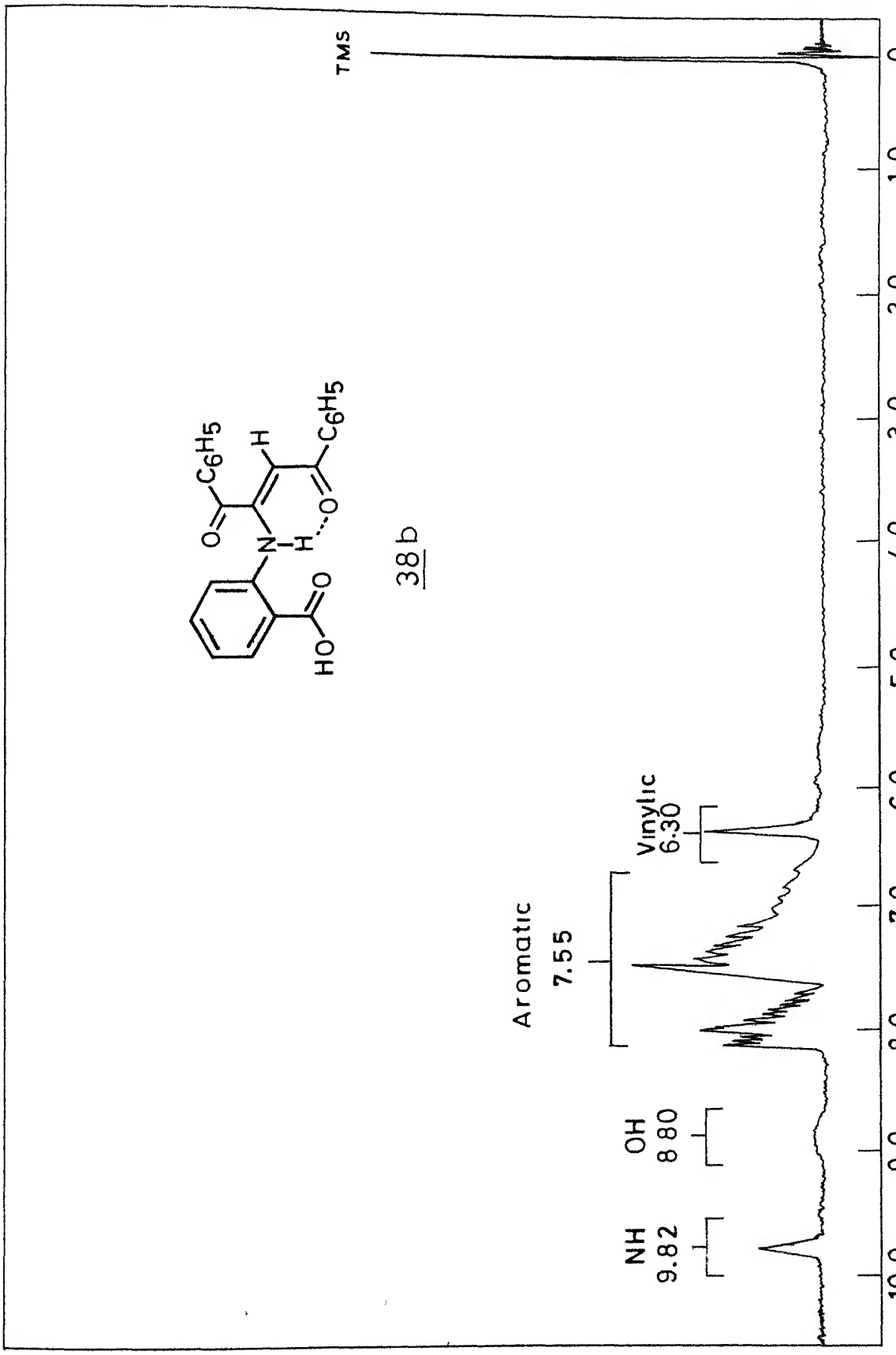


Fig. III 14 NMR spectrum (60 MHz) of 38b

The IR spectrum of 38c, likewise, showed an intramolecularly hydrogen-bonded, NH absorption at 3180 cm^{-1}, whereas the carbonyl absorptions were observed at 1700 and 1680 cm^{-1}, respectively The NMR spectrum of 38c (Fig. III.15) showed a triplet centred around δ 1.33 (3 H) and a quartet centred around δ 4.45 (2 H), which could be assigned to the methyl and methylene protons, respectively of the ester ethoxy group. In addition, the spectrum showed a singlet at δ 6.20 (1 H), assigned to the vinylic proton and a second singlet at δ 11.06 (1 H), which was exchangeable with D_2O and could be assigned to the NH proton. The aromatic protons appeared as a complex multiplet centred around δ 7.31 (14 H).

The UV spectra of 38a, 38b and 38c showed remarkable similarity, as expected and they were characterized by strong absorption maxima around 260, 330 and 390 nm, respectively (Fig. III.16). The UV spectral data of 38a,b,c would suggest that these adducts have the Z-configuration, as far as the stereochemistry across the enamine double bond is concerned.[24-26]

It has been reported that the enamine adducts formed in the reaction of different o-amino substituted nucleophiles with dimethyl acetylenedicarboxylate (DMAD) undergo thermal cyclizations to give the corresponding heterocycles.[27-29] Thus, the enamine adduct formed from the reaction of ethyl anthranilate with DMAD has been reported to give 8-carbeth-oxy-2-carbomethoxy-4(1H)-quinolone, on heating around 250°.[28]

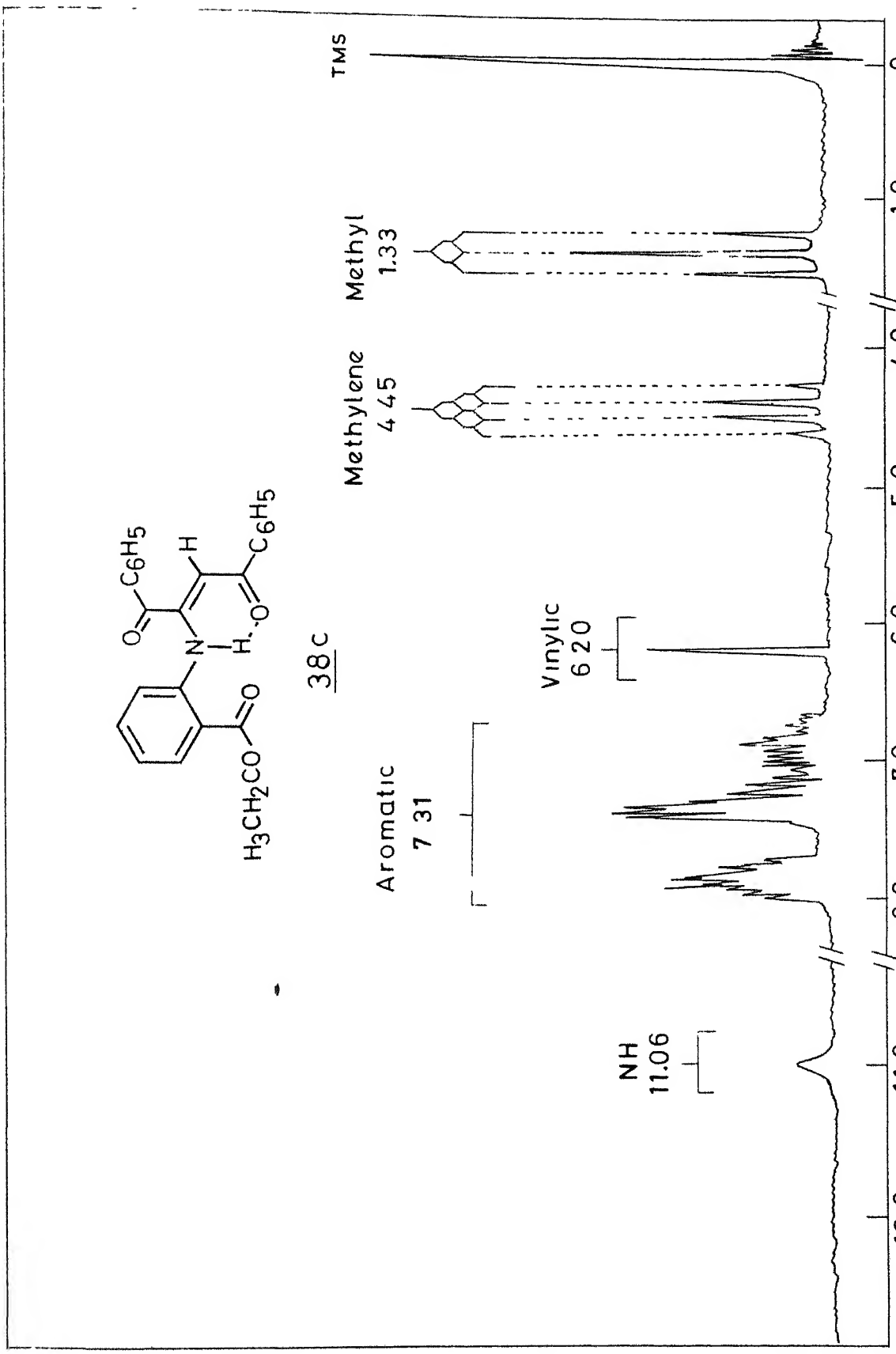


Fig III.15 NMR spectrum (60 MHz) of 38c.

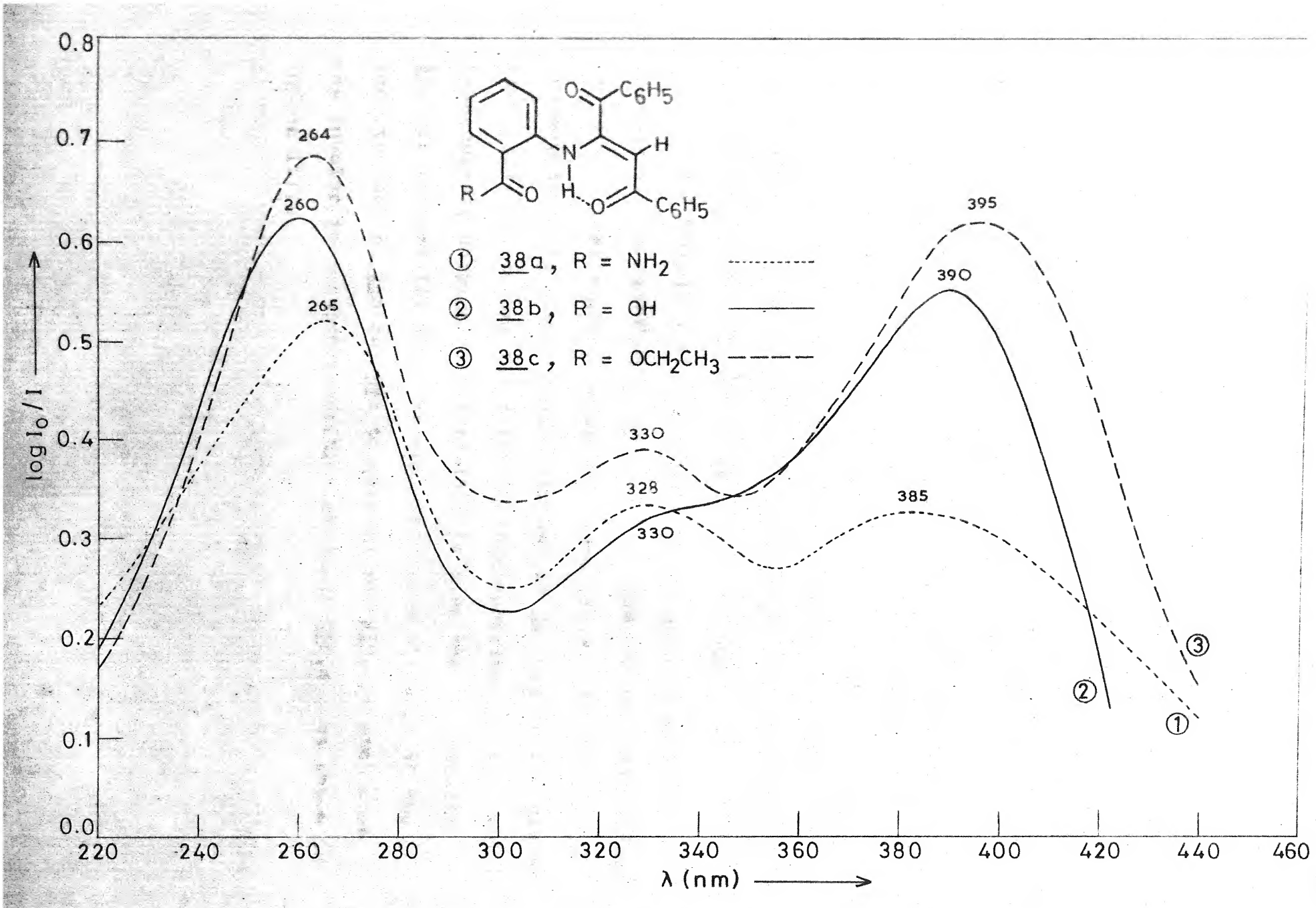


Fig. III. 16 UV spectra of 38a, 38b and 38c in methanol.

In the present studies, attempts have been made to bring about the cyclization of the enamine dione adducts 38b,c, both under thermal and acid-catalyzed conditions. The attempted thermal cyclization of 38c, for example, by heating it to 215° for 4 hr did not give rise to the expected quinolone derivative 37c. In contrast, the attempted cyclization of the adducts, 38b and 38c, under acid-catalyzed conditions gave rise to cleavage products. Thus, the treatment of 38b with methanolic hydrochloric acid, for example, gave a 84% yield of 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (39) and a 54% yield of anthranilic acid (35b). Similarly, the treatment of 38c with methanolic hydrochloric acid gave 75% of 39 and 68% of 35b.

The formation of the enamine dione adducts such as 38a,b,c in the reaction of 35a,b,c with DBA can be rationalized in terms of the pathway shown in Scheme III.9. It has been assumed that the nucleophilic addition of 35a,b,c to DBA gives rise initially to the zwitterionic intermediates 36a,b,c, which subsequently undergo transformation to give the 1:1 adducts, 38a,b,c (Scheme III 9) The acid-catalyzed cleavage of the adducts such as 38b and 38c to give 39 and 35b, in each case may involve the methanol addition products 40b,c , as shown in Scheme III.9.

III.4 EXPERIMENTAL

All melting points are uncorrected and were determined on a Mel-Temp, melting point apparatus. The IR spectra were recorded on Perkin-Elmer Model 377, 521 and/or 580 Infrared spectrophotometers. The electronic spectra were recorded on a Beckmann DB and/or Cary-17D spectrophotometer. NMR traces were recorded on Varian A-60D, Varian HA-100 and/or Jeol 100 MHz spectrometers, using tetramethylsilane (TMS) as internal standard. The mass spectra were recorded on a Hitachi RMU-6E single focussing mass spectrometer or a Varian Mat CH7, mass spectrometer at 70 eV.

III.4.1 Starting Materials

Salicylaldehyde (27a), bp 93° (25 mm), o-hydroxyacetophenone (27b), bp 106° (17 mm) and anthranilic acid (35b), mp 146-147° were obtained as commercial samples and were purified before use. Anthranilamide (35a),[30] mp 110-111°, ethyl anthranilate (35c),[31] bp 145° (15 mm) and dibenzoylacetylene (13),[32] mp 111° were prepared by standard procedures. The petroleum ether used was the fraction, bp 60-80°.

III.4.2 Reaction of Salicylaldehyde (27a) with Dibenzoylacetylene (13) in Acetone

A At Room Temperature

A mixture of salicylaldehyde (27a, 0.122 g, 1 mmol), DBA (0.234 g, 1 mmol) and anhydrous potassium carbonate

(0.138 g, 1 mmol) in acetone (20 ml) was stirred for a period of 3 hr. The inorganic material was removed by filtration and the solvent was removed under vacuum to give a residual mass, which on trituration with a small amount of methanol gave a solid product. Recrystallization of this product from a mixture (2:1) of benzene and petroleum ether gave 0.25 g (68%) of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (30a), mp 137-138°.

Anal. Calcd for $C_{23}H_{16}O_4$: C, 77.54; H, 4.49; Mol. wt., 356. Found: C, 78.03; H, 4.60; Mol. wt., 356 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3464 (ν_{O-H}), 3060 (ν_{C-H}), 1680 and 1660 ($\nu_{C=O}$), 1630, 1600 and 1580 cm^{-1} ($\nu_{C=C}$).

B In Acetone Under Refluxing Conditions

A mixture of 27a (0.122 g, 1 mmol), DBA (0.234 g, 1 mmol) and anhydrous potassium carbonate (0.138 g, 1 mmol) in acetone (20 ml) was refluxed for a period of 4 hr. Subsequent work-up, as in the earlier case, gave a white solid, which on recrystallization from a mixture (3:1) of benzene and petroleum ether gave 0.2 g (58%) of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (29a), mp 170-171°

Anal. Calcd for $C_{23}H_{16}O_4$. C, 77.54; H, 4.49; Mol. wt., 356. Found: C, 77.67; H, 4.27; Mol. wt., 356 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3434 (ν_{O-H}), 1694 and 1634 ($\nu_{C=O}$), 1610 and 1570 cm^{-1} ($\nu_{C=C}$).

III.4.3 Rearrangement of 2,3-Dibenzoyl-4H-1-benzopyran-4-ol (30a) to 2,3-Dibenzoyl-2H-1-benzopyran-2-ol (29a)

A In Refluxing Benzene

A solution of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (90 mg, 0.25 mmol) in benzene (10 ml) was refluxed for a period of ½ hr. Removal of the solvent under reduced pressure gave a white solid, which was recrystallized from a mixture (3:1) of benzene and petroleum ether to give 72 mg (80%) of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (29a), mp 170-171° (mixture melting point).

B In Aqueous Methanolic Hydrochloric Acid

A solution of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (90 mg, 0.25 mmol) and 0.1 N hydrochloric acid (1 ml) in methanol (10 ml) was refluxed for 10 min. Removal of the solvent under vacuum gave a sticky mass, which was dissolved in benzene, washed with water and subsequently dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave 70 mg (77%) of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (29a), mp 170-171° (mixture melting point), after recrystallization from a mixture (3:1) of benzene and petroleum ether.

III.4.4 Generation of 2,3-Dibenzoylbenzopyrylium Ion (33a) and its Reaction with Methanol

A From 2,3-Dibenzoyl-4H-1-benzopyran-4-ol (30a)

A solution of 2,3-dibenzoyl-4H-1-benzopyran-4-ol (0.354 g, 1 mmol) in dry methanol (10 ml) was refluxed for 10 hr with 0.1 N p-toluenesulfonic acid (5 ml). The reaction mixture was cooled and then neutralized with pyridine. After removal of the solvent under vacuum, the residue that was left behind was extracted with ether and the ether-extract was washed with water and dried over anhydrous sodium sulfate. Subsequent removal of the solvent under vacuum gave 0.1 g (28%) of 2,3-dibenzoyl-2-methoxy-2H-1-benzopyran (34a), mp 110°, after recrystallization from methanol.

Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.84; H, 4.86. Found: C, 77.61; H, 4.97.

IR spectrum (KBr) ν_{max}: 3050, 2970 and 2825 (ν_{C-H}, asymmetric and symmetric), 1700 and 1650 ($\nu_{C=O}$), 1630, 1600 and 1570 cm^{-1} ($\nu_{C=C}$).

B From 2,3-Dibenzoyl-2H-1-benzopyran-2-ol (29a)

A solution of 2,3-dibenzoyl-2H-1-benzopyran-2-ol (0.354 g, 1 mmol) in dry methanol (10 ml) was acidified with a small quantity of 98% sulfuric acid and the mixture was refluxed for 20 hr. Subsequent work-up, as in the earlier

case gave 0.15 g (44%) of 2,3-dibenzoyl-2-methoxy-2H-1-benzopyran (34a), mp 110° (mixture melting point), after recrystallization from methanol.

III.4.5 Reaction of o-Hydroxyacetophenone (27b) with Dibenzoylacetylene (13)

A In Acetone at Room Temperature

A mixture of o-hydroxyacetophenone (27b, 0.136 g, 1 mmol), DBA (0.234 g, 1 mmol) and potassium carbonate (0.138 g, 1 mmol) in acetone (20 ml) was stirred at room temperature for a period of ½ hr. The inorganic material was removed by filtration and the mother-liquor was concentrated under vacuum to give an oily substance, which solidified on treatment with a small amount of methanol Recrystallization of the resultant product from a mixture (2:1) of benzene and petroleum ether gave 0.23 g (62%) of 2,3-dibenzoyl-4-methyl-4H-1-benzopyran-4-ol (30b), mp 173-174°.

Anal. Calcd for $C_{24}H_{18}O_4$. C, 77.84; H, 4.86; Mol. wt., 370. Found: C, 78.34; H, 4.73, Mol. wt., 370 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3560 and 3440 (ν_{O-H}, free and hydrogen-bonded), 3060 and 2960 (ν_{C-H}), 1665 and 1630 ($\nu_{C=O}$), 1585, 1565 and 1475 ($\nu_{C=C}$) and 1215 cm^{-1} (ν_{C-O-C}).

B In Acetone Under Refluxing Conditions

A mixture of 27b (0.136 g, 1 mmol), DBA (0.234 g, 1 mmol) and anhydrous potassium carbonate (0.138 g, 1 mmol) in acetone (20 ml) was refluxed for 4 hr. Subsequent work-up, as in the previous case, gave 0.22 g (60%) of 2,3-dibenzoyl-4-methyl-4H-1-benzopyran-4-ol (30b), mp 173-174° (mixture melting point).

C In Tetrahydrofuran at Room Temperature

A mixture of 27b (0.136 g, 1 mmol), DBA (0.234 g, 1 mmol) and anhydrous potassium carbonate (0.138 g, 1 mmol) in THF (20 ml) was stirred at room temperature for 4 hr. Subsequent work-up in the usual manner gave 0.27 g (73%) of 30b, mp 173-174° (mixture melting point), after recrystallization from a mixture (2:1) of benzene and petroleum ether.

III.4.6 Reaction of Anthranilamide (35a) with Dibenzoylacetylene (1J)

A In Methanol at Room Temperature

A mixture of anthranilamide (35a, 0.136 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was stirred at room temperature for ½ hr. Removal of the solvent under vacuum and recrystallization of the resultant residue from ethanol gave 0.33 g (89%) of 1,4-diphenyl-2-(N-2-carboxamidophenylamino)but-2-ene-1,4-dione (38a), mp 169°.

Anal. Calcd for $C_{23}H_{18}N_2O_3$: C, 74.59; H, 4.86; N, 7.56; Mol. wt., 370. Found: C, 75.02; H, 4.48; N, 7.72; Mol. wt., 370 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3440 and 3320 (ν_{N-H}, amide, asymmetric and symmetric), 3200 (ν_{N-H}, intramolecularly hydrogen-bonded), 3045 (ν_{C-H}), 1670 and 1640 ($\nu_{C=O}$), 1600, 1570 and 1530 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 265 nm (ε, 12,300), 328 (7,700) and 385 (7,600).

B In Tetrahydrofuran Under Refluxing Conditions

A mixture of 35a (0.136 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was refluxed for 16 hr. Work-up of the reaction mixture in the usual manner gave 0.3 g (81%) of 1,4-diphenyl-2-(N-2-carboxamidophenylamino)-but-2-ene-1,4-dione (38a), mp 169° (mixture melting point), after recrystallization from ethanol.

III.4.7 Reaction of Anthranilic Acid (35b) with Dibenzoylacetylene (13)

A In Methanol at Room Temperature

A mixture of anthranilic acid (35b, 0.137 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (20 ml) was stirred at room temperature for 4 hr, during which period an yellow solid precipitated out. The solid material was removed by

filtration and recrystallized from a mixture (2:1) of benzene and petroleum ether to give 0.34 g (90%) of 1,4-diphenyl-2-(N-carboxyphenylamino)but-2-ene-1,4-dione (38b), mp 184°.

Anal. Calcd for $C_{23}H_{17}NO_4$: C, 74.39; H, 4.58; N, 3.77. Found: C, 74.27; H, 4.29; N, 3.77.

IR spectrum (KBr) ν_{max}: 3200-2500 (broad band, ν_{O-H} and ν_{N-H}, hydrogen-bonded), 1680 and 1660 ($\nu_{C=O}$), 1615, 1590, 1575 and 1550 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 260 nm (ε, 19,500), 330 (9,800, sh) and 390 (16,300).

B In Tetrahydrofuran Under Refluxing Conditions

A mixture of 35b (0.137 g, 1 mmol) and DBA (0.234 g, 1 mmol) in THF (20 ml) was refluxed for 12 hr. Subsequent work-up, as in the earlier case gave 0.25 g (67%) of 38b, mp 184° (mixture melting point), after recrystallization from a mixture (2:1) of benzene and petroleum ether.

C In Xylene Under Refluxing Conditions

A mixture of 35b (0.137 g, 1 mmol) and DBA (0.234 g, 1 mmol) in xylene (15 ml) was refluxed for 3 hr. Removal of the solvent under reduced pressure gave an oily residue, which solidified on treatment

with a small amount of methanol. Recrystallization of this product from a mixture (2:1) of benzene and petroleum ether gave 0.33 g (88%) of 1,4-diphenyl-2-(N-2-carboxyphenylamino)-but-2-ene-1,4-dione (38b), mp 184° (mixture melting point).

III.4.8 Reaction of 1,4-Diphenyl-2-(N-2-carboxyphenylamino)but-2-ene-1,4-dione (38b) with Methanolic-Hydrochloric Acid

A solution of 38b (0.5 g, 1.35 mmol) in methanol (10 ml) containing 0.5 ml of concentrated hydrochloric acid was refluxed for 1 hr. Removal of the solvent under vacuum gave an oily mass, which was extracted with ether and subsequently washed with water Removal of the solvent from the organic layer gave a solid residue, which was recrystallized from methanol to give 0.3 g (84%) of 1,4-diphenyl-2-methoxy-but-2-ene-1,4-dione (39), mp 108° (mixture melting point and superimposable IR) [33]

The aqueous layer was neutralized with the requisite amount of sodium bicarbonate and was extracted with methylene chloride. Removal of the solvent from the methylene chloride-extract gave a residual product, which was recrystallized from ethanol to give 100 mg (54%) of anthranilic acid (35b), mp 146-147° (mixture melting point).

III.4.9 Reaction of Ethyl Anthranilate (35c) with Dibenzoylacetylene (13)

A In Methanol Under Refluxing Conditions

A mixture of ethyl anthranilate (35c, 0.165 g, 1 mmol) and DBA (0.234 g, 1 mmol) in methanol (15 ml) was refluxed for ½ hr. On cooling, an yellow solid separated out, which was filtered off and recrystallized from ethanol to give 0.34 g (85%) of 1,4-diphenyl-2-(N-2-ethoxycarbonylphenylamino)-but-2-ene-1,4-dione (38c), mp 135-136°.

Anal. Calcd for $C_{25}H_{21}NO_4$: C, 75.18; H, 5.27; N, 3.51. Found: C, 74.79; H, 4.97; N, 3.85.

IR spectrum (KBr) ν_{max}: 3180 (ν_{N-H}, intramolecularly hydrogen-bonded), 3045, 2970 and 2890 (ν_{C-H}, asymmetric and symmetric), 2925 and 2860 (ν_{CH_2}, asymmetric and symmetric), 1700 ($\nu_{C=O}$, ester), 1680 ($\nu_{C=O}$), 1610, 1570 and 1550 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 260 nm (ε, 20,100), 330 (11,000) and 395 (17,800).

B In Toluene Under Refluxing Conditions

A mixture of 35c (0.165 g, 1 mmol) and DBA (0.234 g, 1 mmol) was refluxed in toluene (15 ml) for 4 hr. Removal of the solvent under reduced pressure gave

an oily substance, which was passed through a small alumina column. Elution with petroleum ether gave 0.28 g (70%) of 38c, mp 135-136° (mixture melting point), after recrystallization from ethanol.

III.4.10 Attempted Thermolysis of 1,4-Diphenyl-2-(N-2-ethoxycarbonylphenylamino)but-2-ene-1,4-dione (38c)

A sample of 38c (0.1 g, 0.25 mmol) was heated in a sealed tube around 210-215° for 4 hr. The residue, on recrystallization from ethanol gave 95 mg (95%) of the unchanged starting material (38c), mp 135-136° (mixture melting point).

III.4.11 Reaction of 1,4-Diphenyl-2-(N-2-ethoxycarbonylphenylamino)but-2-ene-1,4-dione (38c) with Methanolic Hydrochloric Acid

A solution of 38c (0.5 g, 1.25 mmol) in methanol (10 ml) was mixed with 0.5 ml of hydrochloric acid and refluxed for 1 hr. Removal of the solvent under reduced pressure gave an oily residue, which was extracted with ether and the organic layer was washed with water. Removal of the solvent from the ether-extract gave 0.25 g (75%) of 1,4-diphenyl-2-methoxybut-2-ene-1,4-dione (39), mp 108° (mixture melting point and superimposable IR),[33] after recrystallization from methanol.

The aqueous layer was neutralized with the requisite amount of sodium bicarbonate and subsequently extracted with methylene chloride. Removal of the solvent from the methylene chloride extract gave 115 mg (68%) of anthranilic acid (35b), mp 146-147° (mixture melting point and superimposable IR).

III.5 REFERENCES

1. R. L. Bol'shedvorskaya and L. I. Vereshchagin, Russian Chem. Rev., 42, 225 (1973).

2. See, Chapter I and Chapter II of this thesis and references cited therein

3. K. Bowden, E. A. Braude and E. R. H. Jones, J. Chem. Soc., 945 (1946).

4. R. Gelin and D. Makula, Bull. Soc. Chim. France, 2347 (1966)

5. L. I. Vereshchagin, E. I. Titova, T. V. Lipovich and L. D. Gavrilov, Zhur. Org. Khim., 7, 903 (1971); Chem. Abstr., 75, 63317 (1971).

6. L. I. Vereshchagin, N. V. Sushkova, S. R. Buzilova and E. I. Titova, Dokl. Vses. Konf. Khim. Atsetilena, 1, 173 (1972); Chem. Abstr., 79, 91901 (1973).

7. P. S. Venkataramani, N. K. Saxena, V. K. Tripathi and G. Mehta, Indian J Chem., 852 (1975).

8. L. I. Vereshchagin, L. D. Gavrilov, R. L. Bol'shedvorskaya, E. I. Titova, S. R. Buzilova, A. V. Maksikova and G. A. Kalabin, Zhur. Org. Khim., 10, 2059 (1974); Chem. Abstr., 82, 43338 (1975).

9. S. Lahiri, M. P. Mahajan, R. Prasad and M. V. George, Tetrahedron, 33, 3159 (1977).

10. W. Ried and E. Koenig, Justus Liebigs Ann. Chem., 24 (1972); Chem. Abstr , 76, 140748 (1972).

11. S. P. Korshunov, V. M. Kazantseva, L. A. Vopilina, V. S. Pisareva and N. V. Utekhina, Khim. Geterotsikl. Soedin., 1421 (1973); Chem. Abstr., 80, 27225 (1974).

12. R. L. Amey and N. D. Heindel, Org. Prep. Proced. Int., 8, 306 (1976); Chem. Abstr., 86, 155623 (1977).

13. W. Ried and R. Teubner, Justus Liebigs Ann. Chem., 741 (1978); Chem. Abstr., 89, 109402 (1978).

14. A. P. Bindra and E. LeGoff, Tetrahedron Lett., 1523 (1974)

15. R. G. Bass, D D. Crichton, H. K. Meetz and A. F. Johnson, Tetrahedron Lett., 2073 (1975).

16. V Rosnati and A. Salimbeni, Gazz. Chim. Ital., 107, 271 (1977); Chem. Abstr., 88, 104306 (1978).

17. E. Manghisi and A Salimbeni, Ger. Patent, 2,502,938; Chem. Abstr., 83, 147303 (1975).

18. V. N. Elokhina, A. S. Nakhmanovich, I D. Kalikhman, N. P Sokol'nikova and M. G. Voronkov, Khim. Geterotsikl Soedin., 1328 (1975); Chem. Abstr., 84, 43912 (1976).

19. V. N. Elokhina, A. S. Nakhmanovich, I. D. Kalikhman and M. G. Voronkov, Tezisy Dokl.-Vses. Konf. Khim. Atsetilena, 5th, 298 (1975); Chem. Abstr., 88, 170015 (1978).

20. M. N. Basyouni, M. T. Omar and E. A. Ghali, Synthesis, 115 (1980).

21. K. T. Potts and A. J. Elliott, J. Org. Chem., 38, 1769 (1973).

22. R. K. Gupta and M. V. George, Tetrahedron, 31, 1263 (1975).

23. D. H. Williams and I. Fleming, "Spectroscopic Methods in Organic Chemistry", McGraw-Hill, London, 1973, p. 51.

24. S. Lahiri, Ph.D. Thesis, Indian Institute of Technology, Kanpur, 1977.

25. R. Huisgen, K. Herbig, A. Siegl and H. Huber, Chem. Ber., 99, 2526 (1966).

26. E. Winterfeldt and H. Preuss, Chem Ber., 99, 450 (1966).

27. E. C. Taylor and N. D. Heindel, J. Org. Chem., 32, 3339 (1967).

28. S. K. Khetan, J. G. Hiriyakkanavar and M. V. George, Tetrahedron, 24, 1567 (1968).

29. S. K. Khetan and M. V. George, Can. J. Chem., 47, 3545 (1969).

30. A. Reissert and F. Grube, Chem. Ber., 42, 3710 (1909).

31. E. Erdmann and H. Erdmann, Chem. Ber., 32, 1213 (1899).

32. R. E. Lutz and W. R. Smithey, J. Org. Chem., 16, 51 (1951).

33. J. B. Conant and R. E. Lutz, J. Am. Chem. Soc., 47, 881 (1925).

CHAPTER IV

PHOTOCHEMICAL TRANSFORMATIONS OF SOME ENAMINE DIONES AND RELATED SYSTEMS

IV.1 ABSTRACT

Photochemical transformations of a few enamine diones such as 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18), 1,4-diphenyl-2-(N-methyl-N-phenylamino)but-2-ene-1,4-dione (19) and 1,4-diphenyl-2-piperidinobut-2-ene-1,4-dione (20) have been attempted. Irradiation of 18 in methanol, for example, either in a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) or employing a 450-W Hanovia medium-pressure mercury lamp, led

to the recovery of the starting material. Similarly, enamine diones, carrying a cis-1,2-dibenzoylalkene chromophore, such as 19 and 20 did not undergo any appreciable change, on irradiation. Attempts to prepare the N-benzoyl and N-acetyl derivatives of enamine diones such as 18 resulted in the formation of the corresponding enol esters. Thus, benzoylation of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18) gave a 78% yield of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23), whereas acetylation of 18, under analogous conditions gave a 76% yield of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)-but-3-en-1-one (24). Similarly, the benzoylation of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21) gave a 60% yield of 4-benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one (25).

Irradiation of the enol benzoate 23 in methanol, using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a mixture of products consisting of 1,4-diphenyl-4-methoxy-2-(N-phenylimino)but-3-en-1-one (27, 75%) and benzoic acid (65%). It was shown in a separate experiment, that the mere refluxing of 23 in methanol also gives rise to the enol ether 27 (70%). In contrast, the irradiation of a solution of 23 in methanol using a 450-W Hanovia medium-pressure mercury lamp gave a mixture of products consisting of the enamine dione 18 (40%), 1,4-diphenyl-3-methoxy-2-(N-phenylamino)but-2-ene-1,4-dione (34a, 19%) and

benzoic acid (50%). On the other hand, irradiation of a benzene solution of 23, under analogous conditions, gave a mixture of 18 (61%) and benzoic acid (24%).

Irradiation of a methanol solution of the enol acetate 24, using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a 60% yield of the enol ether 27, whereas the irradiation of 24 using a 450-W Hanovia medium-pressure mercury lamp gave a 34% yield of the deacetylated product 18. In contrast, the irradiation of a benzene solution of 24 did not result in any photoconversion. Similarly, the irradiation of a methanol solution of the enol benzoate 25, using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a mixture of the enamine dione 21 (76%) and benzoic acid (83%). Likewise, the irradiation of 25 in methanol using a 450-W Hanovia medium-pressure mercury lamp gave a mixture of 21 (73%) and benzoic acid (51%).

In continuation of our studies, we have examined the photochemical transformations of some enehydrazine diones such as 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (35a) and 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (35b). Irradiation of a solution of 35a in methanol, using a 450-W Hanovia medium-pressure mercury lamp gave a 63% yield of 4,5-dibenzoyl-1,3-diphenylpyrazole (38a), whereas the irradiation of 35a in benzene,

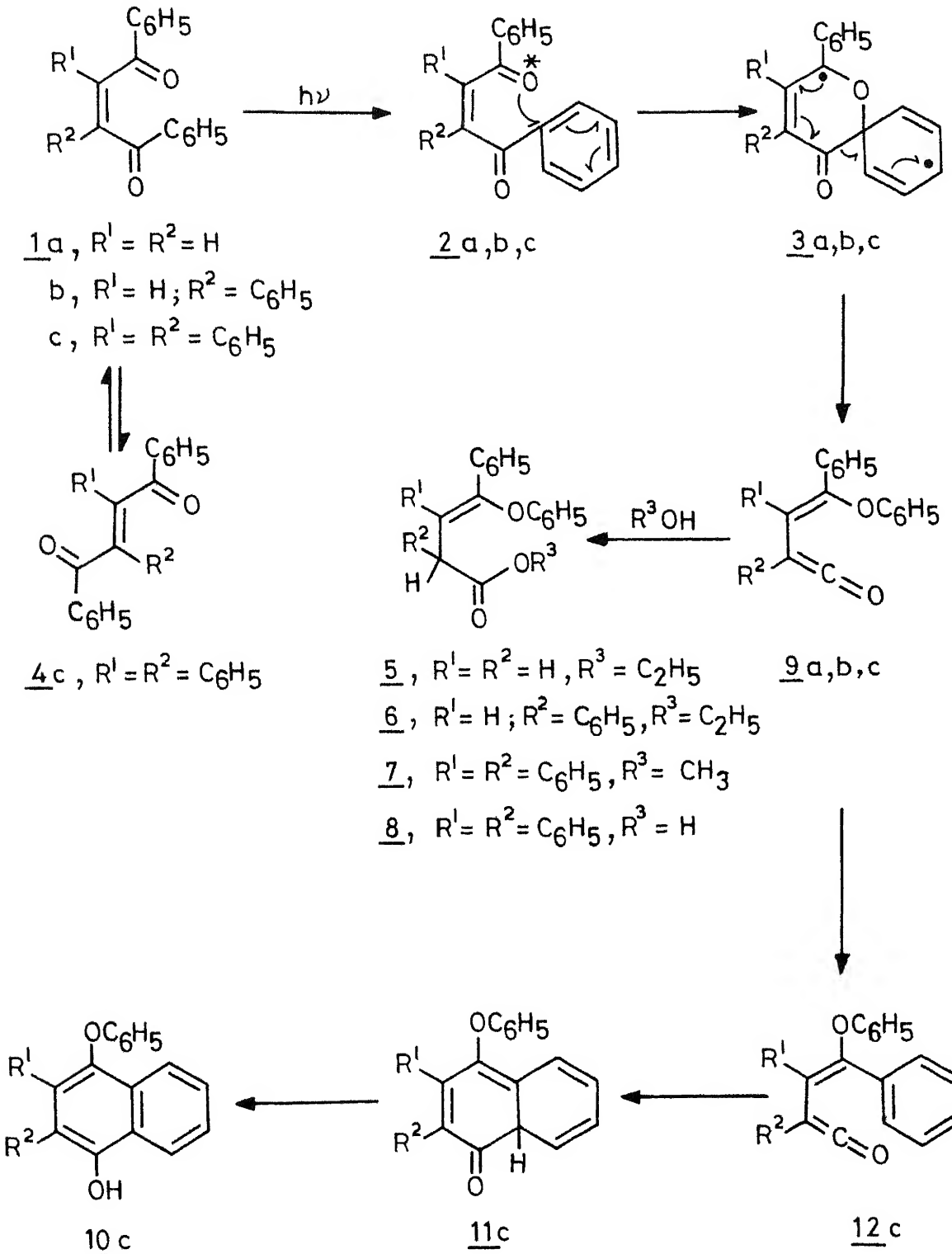
under analogous conditions, gave a 77% yield of 38a. Similarly, the irradiation of 35b in methanol gave a 33% yield of 3-(p-anisyl)-4,5-dibenzoyl-1-phenylpyrazole (38b).

Reasonable mechanisms have been suggested to account for the formation of the different products in the phototransformations of 23, 24, 25, 35a and 35b.

IV.2 INTRODUCTION

1,2-Dibenzoylethylenes (1a-c) are reported to undergo interesting photorearrangements in protic solvents such as alcohols, giving rise to the corresponding esters (5-7)[1,2] (Scheme IV.1). Thus, it has been observed that the photolysis of cis-1,2-dibenzoylethylene (1a) in ethanol leads to the formation of ethyl 4-phenyl-4-phenoxy-3-butenoate (5). Similar transformations have been observed in the case of dibenzoylstyrene (1b) and dibenzoylstilbene (1c), leading to the formation of the corresponding esters 6 and 7, respectively. Padwa et al.[3] have shown that the photolysis of trans-dibenzoylstilbene (4c) gives rise to different products, depending upon the nature of the solvent employed. The irradiation of 4c in benzene, for example, gives a mixture of products consisting of cis-dibenzoylstilbene (1c) and 1-hydroxy-2,3-diphenyl-4-phenoxynaphthalene (10 whereas 2,3,4-triphenyl-4-phenoxy-3-butenoic acid (8) is formed in aqueous dioxane. Mention may be made in this connection that

Scheme IV.1



1a, $R^1 = R^2 = H$

b, $R^1 = H$; $R^2 = C_6H_5$

c, $R^1 = R^2 = C_6H_5$

2a,b,c

3a,b,c

4c, $R^1 = R^2 = C_6H_5$

5, $R^1 = R^2 = H$, $R^3 = C_2H_5$

6, $R^1 = H$; $R^2 = C_6H_5$, $R^3 = C_2H_5$

7, $R^1 = R^2 = C_6H_5$, $R^3 = CH_3$

8, $R^1 = R^2 = C_6H_5$, $R^3 = H$

9a,b,c

10c

11c

12c

Sugiyama and Kashima[4] have observed that the photolysis of 1,2-dibenzoylethylene (1a) in acidic methanol results in the formation of a mixture of products consisting of methyl 2,3,4-triphenyl-4-phenoxy-3-butenoate (7), 1,2-dibenzoyl-1-methoxyethane and 2,5-diphenylfuran.

Zimmerman et al.[5] had suggested that the phototransformations of dibenzoylethylenes 1a-c, giving rise to the corresponding esters 5-7, can be rationalized in terms of the pathway shown in Scheme IV.1. On the basis of detailed quenching studies, these workers had suggested that the phototransformations of dibenzoylethylenes proceed primarily from their excited singlet states.

In the photoreactions of dibenzoylalkenes, it has been generally observed that a major photochemical pathway involves the cis-trans isomerization of the alkene double bond. In recent studies,[6,7] however, it has been shown that substrates, wherein the cis-trans isomerization possibility is prevented through structural constraints, undergo the expected photorearrangement almost exclusively. Thus, it has been observed that the photolysis of a cis-1,2-dibenzoylalkene system such as 2,3-dibenzoylbicyclo[2.2.2]oct-2-ene (13) in benzene, for example, gives rise to a mixture of products consisting of 3-(phenoxyphenylmethylene)bicyclo[2.2.2]octane-2-carboxylic acid (14a, 7%) and the lactone 15 (20%). On the other hand,

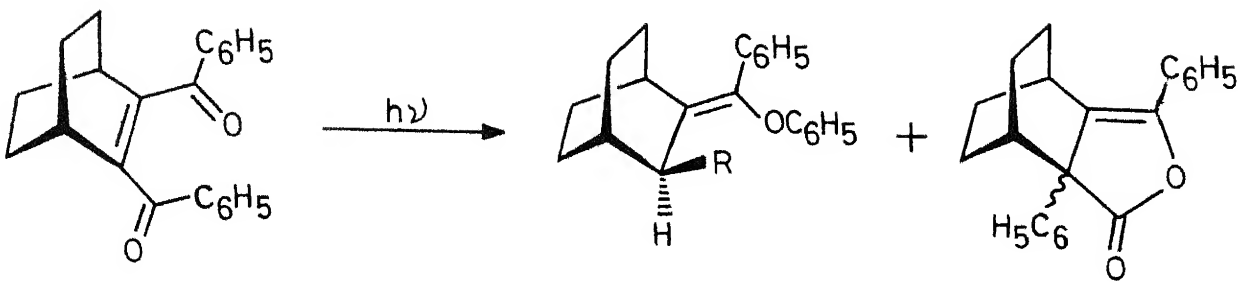
irradiation of 13 in methanol gave the methyl ester 14b (20%). Similarly, irradiation of the bicyclic enedione 16 in benzene and methanol gave the corresponding carboxylic acid 17a (15%) and the ester 17b (41%), respectively (Scheme IV.2).

The object of the present investigation has been to examine the photochemical transformations of a few enamine diones, containing 1,2-dibenzoylalkene chromophores, with a view to studying the nature of the products formed in these reactions and also to understand their mechanisms.

IV.3 RESULTS AND DISCUSSION

The enamine diones that we have examined in the present investigations, namely, 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18),[8] 1,4-diphenyl-2-(N-methyl-N-phenylamino)-but-2-ene-1,4-dione (19),[9] 1,4-diphenyl-2-piperidinobut-2-ene-1,4-dione (20),[8] 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (35a)[10] and 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (35b)[10] were prepared by the reaction of the appropriate nitrogen-containing nucleophiles with DBA, as per reported procedures. Irradiation of a methanol solution of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18) using either a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) or a 450-W Hanovia medium-pressure mercury lamp did not result in any appreciable change; the starting

Scheme IV.2

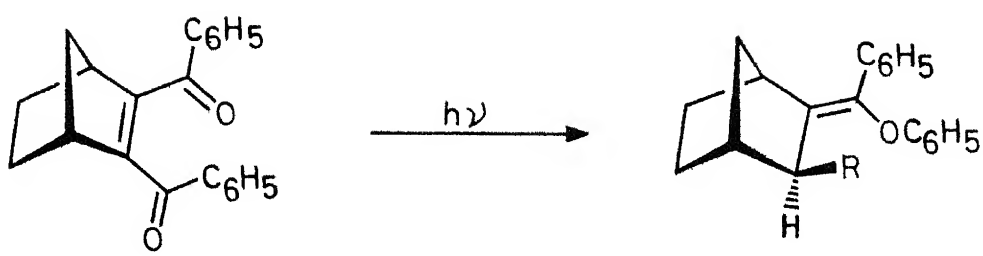


13

14 a , R = COOH

b , R = $COOCH_3$

15



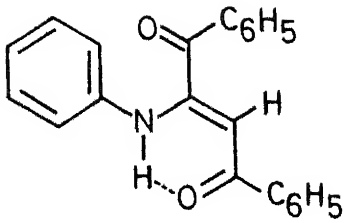
16

17 a , R = COOH

b , R = $COOCH_3$

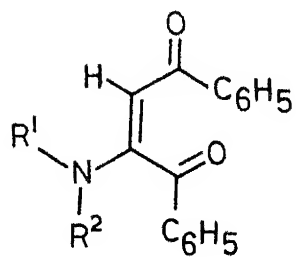
material was recovered in each case (Scheme IV.3). It is not clear whether the strong hydrogen-bonding in 18 prevents the cis-trans isomerization around the alkene double bond and thereby retard the formation of cis-isomer, needed for subsequent photo-transformations. To examine this possibility, we have attempted the phototransformations of two enamine diones such as 1,4-diphenyl-2-(N-methyl-N-phenylamino)but-2-ene-1,4-dione (19) and 1,4-diphenyl-2-piperidinobut-2-ene-1,4-dione (20), containing tertiary substituted nitrogen atoms. Irradiation of 19 in methanol using either a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) or a 450-W Hanovia medium-pressure mercury lamp resulted in the recovery of the unchanged starting material in each case. Similarly, the irradiation of 20 in methanol for 10 hr did not result in any appreciable change. It appears that the nitrogen substitution on the 1,2-dibenzoylalkene moiety is bringing about the deactivation of the excited state, thereby preventing the expected rearrangement. To assess whether the presence of electron-withdrawing groups such as benzoyl and acetyl on the nitrogen atom of the enamine dione moiety 18, would lead to any discernible photochemistry, an attempt has been made to prepare the benzoyl and acetyl derivatives of 18. An attempted benzoylation of 18 by treatment with benzoyl chloride and pyridine resulted in the formation of a 78% yield of a product, identified as 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one

Scheme IV.3



$h\nu$, CH_3OH → No reaction

18



$h\nu$, CH_3OH → No reaction

19 , $R^1 = C_6H_5$, $R^2 = CH_3$

20 , R^1, $R^2 = -(CH_2)_5-$

(23) (Scheme IV.4). Similarly, acetylation of 18, under analogous conditions gave a 76% yield of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24). Likewise, the benzoylation of the enamine dione, 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21) gave a 60% yield of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (25) (Scheme IV.4). The enamine dione 21 itself was prepared in a 67% yield through the nucleophilic addition of p-toluidine to DBA. The structures of all the compounds, 21, 23, 24 and 25 have been arrived at on the basis of analytical results and spectral data.

The IR spectrum of 21, for example, showed an intramolecularly hydrogen-bonded NH absorption at 3180 cm^{-1} and a carbonyl absorption at 1670 cm^{-1}. The NMR spectrum of 21 (Fig. IV.1) showed a singlet at δ 2.17 (3 H) due to the methyl group and a second singlet at δ 6.00 (1 H) due to the vinylic proton and yet another singlet at δ 12.52 (1 H, D_2O-exchangeable) due to the hydrogen-bonded NH proton. In addition, the spectrum showed a complex multiplet centred around δ 7.45 (14 H) due to the aromatic protons.

The IR spectrum of 23 showed two carbonyl absorption at 1740 and 1655 cm^{-1}, assigned to the ester and benzoyl carbonyls, respectively. The NMR spectrum of 23 (Fig. IV.2) showed a singlet at δ 6.30 (1 H), assigned to the vinylic proton and a complex multiplet centred around δ 7.50 (20 H), assigned to the

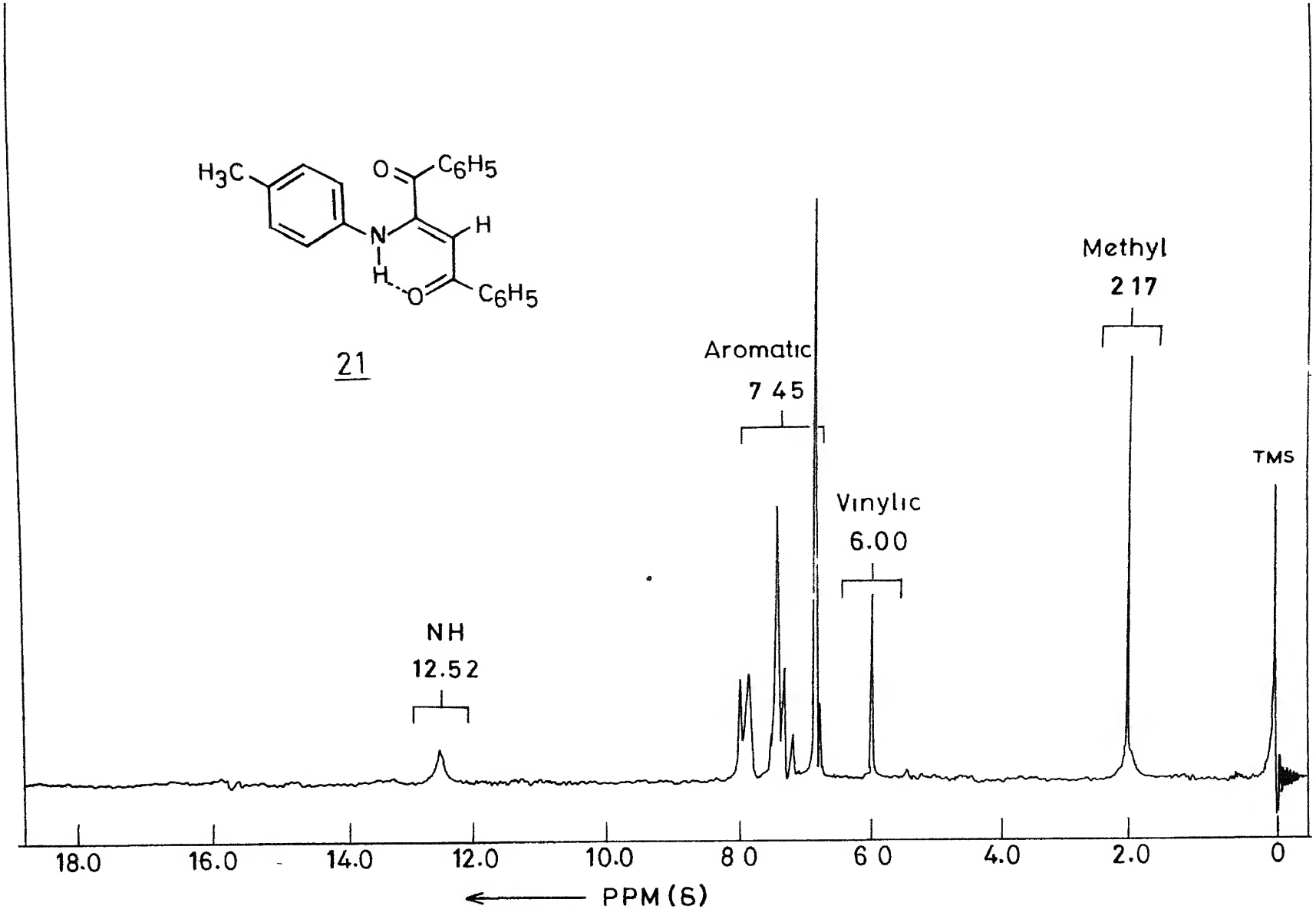
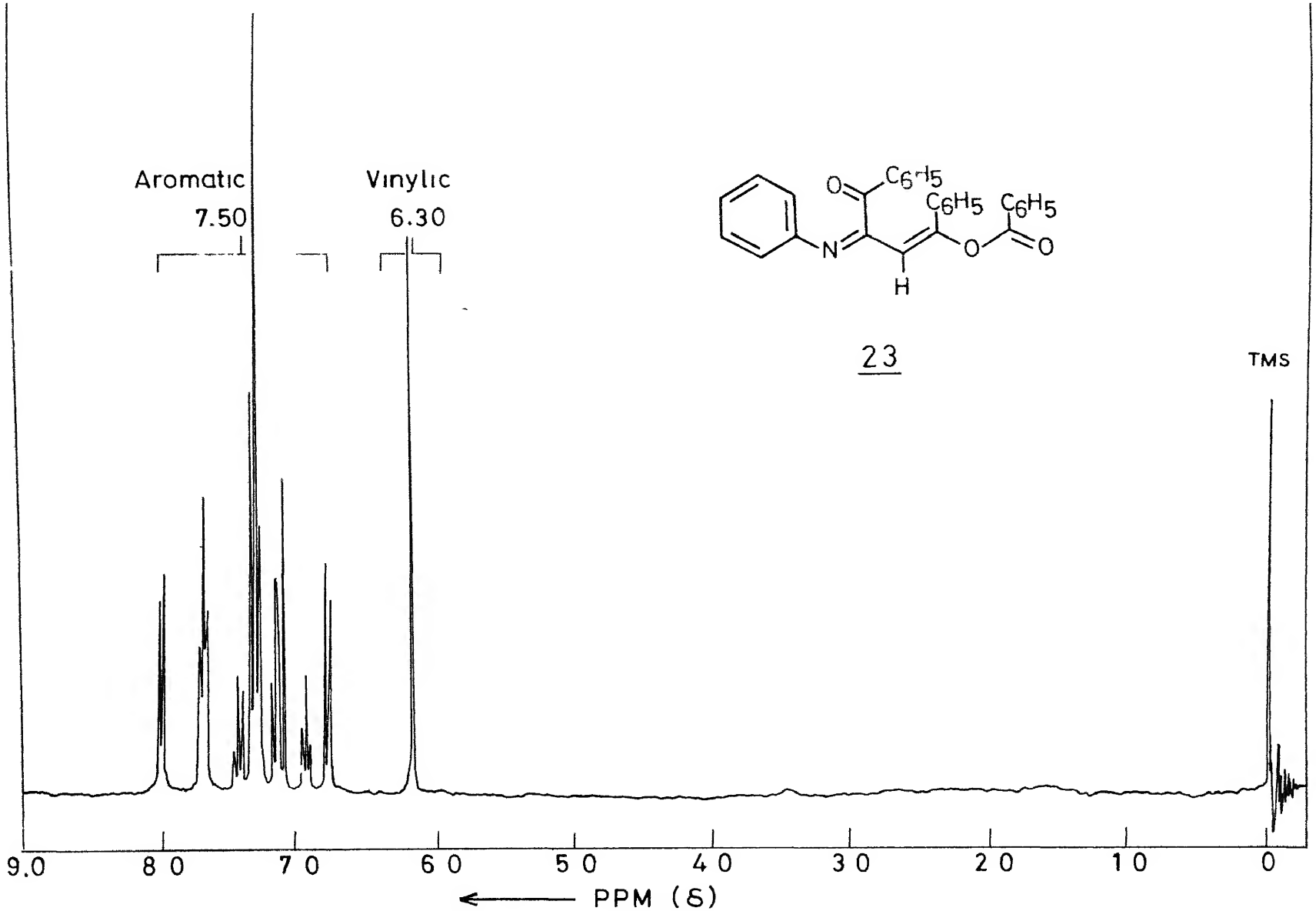


Fig. IV. 1 NMR spectrum (60 MHz) of 21.



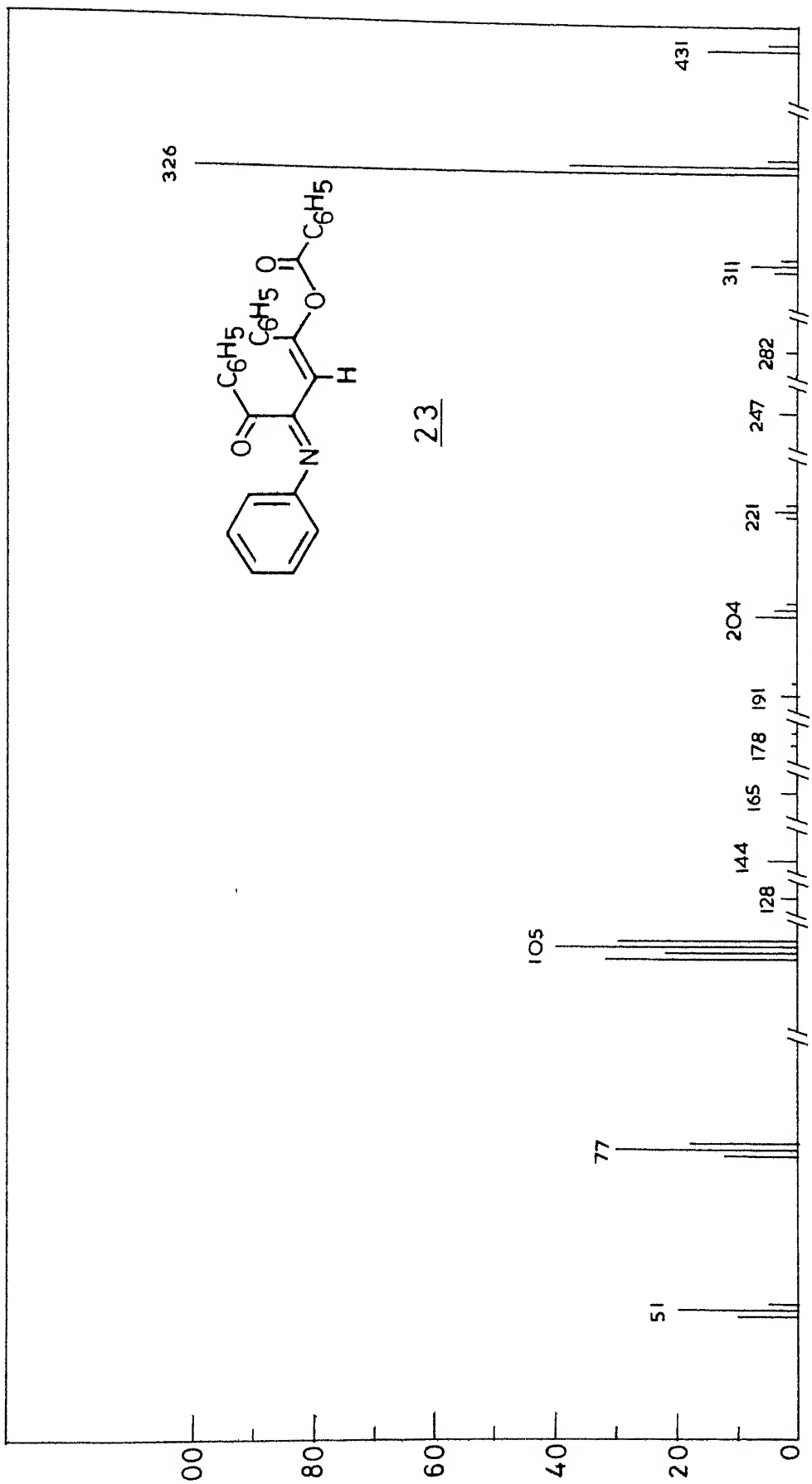
23

Fig. IV. 2 NMR spectrum (270 MHz) of 23.

aromatic hydrogens. The mass spectrum of 23 (Fig. IV.3) showed a molecular ion peak at m/e 431 (15). Other peaks in the spectrum were observed at m/e 326 (100), 310 (4), 282 (2), 247 (3), 222 (2), 221 (4), 220 (4), 206 (2), 205 (4), 204 (8), 193 (1), 191 (2), 178 (1), 165 (2), 145 (6), 144 (6), 105 (40), 103 (36), 77 (30) and 51 (20). Some of the prominent fragmentation patterns of 23 are shown in Scheme IV.5.

The IR spectrum of 24, likewise, showed two carbonyl absorptions at 1760 and 1660 cm^{-1}, respectively, due to the ester and benzoyl groups. The NMR spectrum of 24 (Fig. IV.4) showed a singlet at δ 2.25 (3 H) due to the methyl protons of the acetyloxy group and a second singlet at δ 6.25 (1 H), assigned to the vinylic proton. In addition, the spectrum showed a complex multiplet centred around δ 7.32 (15 H), assigned to the aromatic protons. Further evidence for the structure of 24 was derived from its mass spectrum. The mass spectrum of 24 (Fig. IV.5) showed a molecular ion peak at m/e 369 (30). Other signals in the spectrum were observed at m/e 328 (3), 326 (6), 310 (9), 309 (5), 282 (2), 264 (75), 221 (100), 204 (8), 191 (4), 187 (5), 144 (9), 128 (3), 116 (6), 105 (29), 77 (23) and 51 (5). Some of the probable fragmentation patterns of 24 are shown in Scheme IV.6.

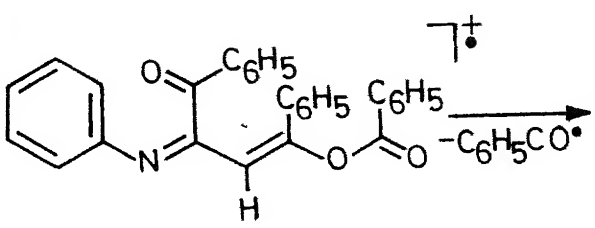
Similarly, the IR spectrum of 25 showed two carbonyl absorptions at 1740 and 1650 cm^{-1}, respectively, due to the ester



23

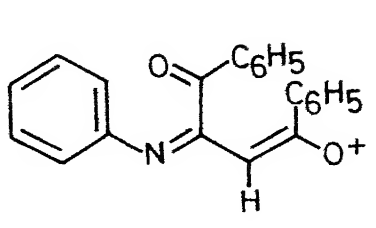
Fig. IV 3 Mass spectrum of 23.

Scheme IV.5



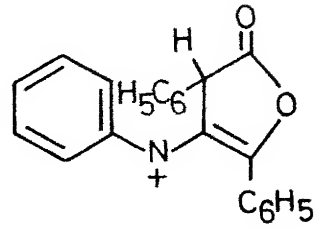
m/e 431(15)

23a



m/e 326(100)

23b



m/e 326(100)

23c

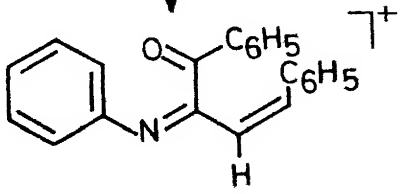
$-CO_2$

$C_{21}H_{16}N^{+}$

m/e 282(2)

23d

$-C_6H_5CO_2^{\bullet}$



m/e 310(4)

23e

$-C_6H_5CO^{\bullet}$

$C_{15}H_{11}NO^{+\bullet}$

m/e 221 (4)

23f

$-C_6H_5^{\bullet}$

$C_{14}H_{10}^{+\bullet}$

m/e 178(1)

23g

$-HCN$

$C_{15}H_{11}N^{+\bullet}$

m/e 205(4)

23h

$-C_6H_5^{\bullet}$

$-CO$

$-H^{\bullet}$

$C_9H_6NO^{+}$

m/e 144(6)

23i

$C_{14}H_{11}N^{+\bullet}$

m/e 193(1)

23j

$C_6H_5-C\equiv O^{+}$

m/e 105 (40)

23k

$C_{15}H_{10}N^{+}$

m/e 204(8)

23l

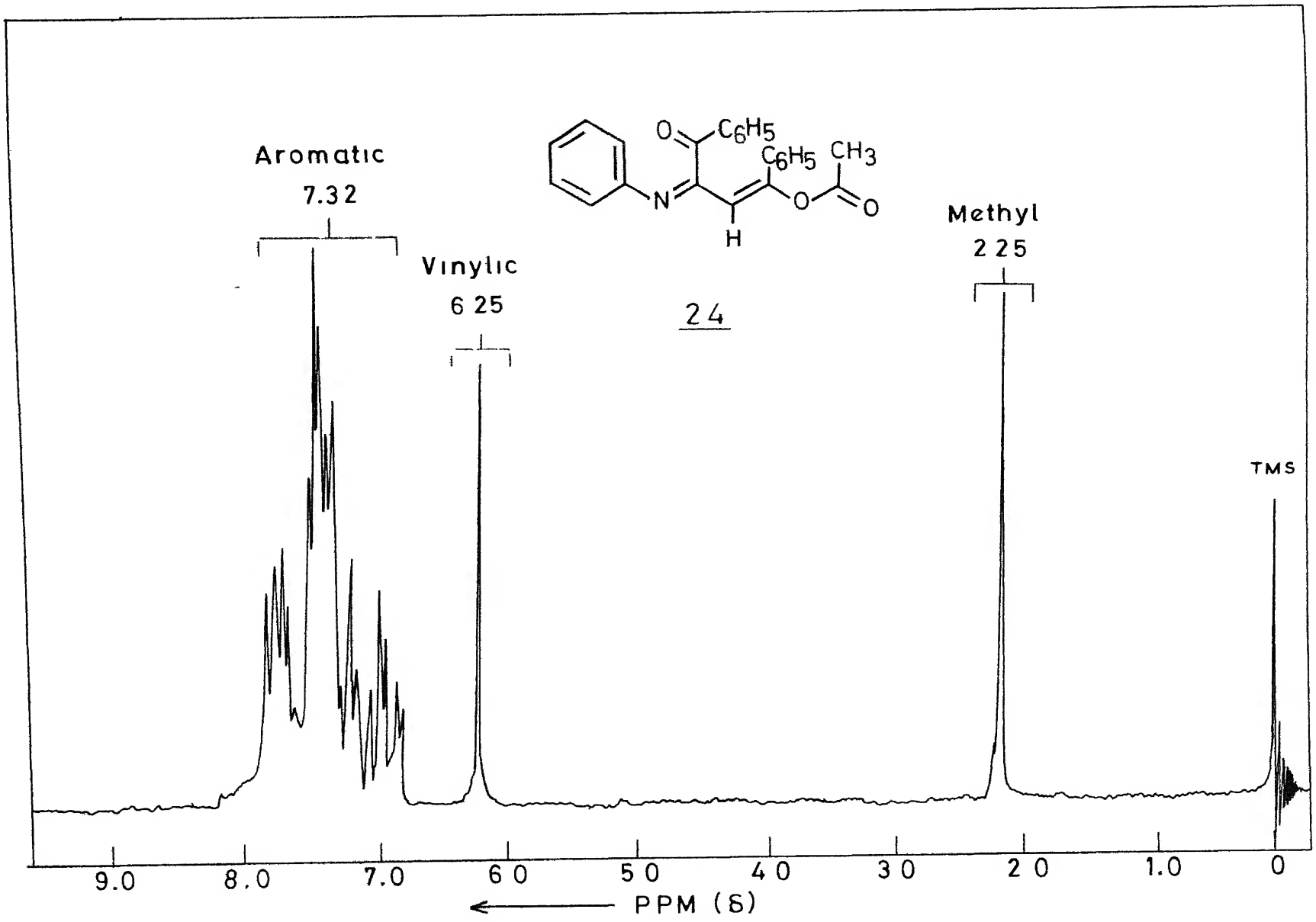


Fig IV . 4 NMR spectrum (60 MHz) of 24

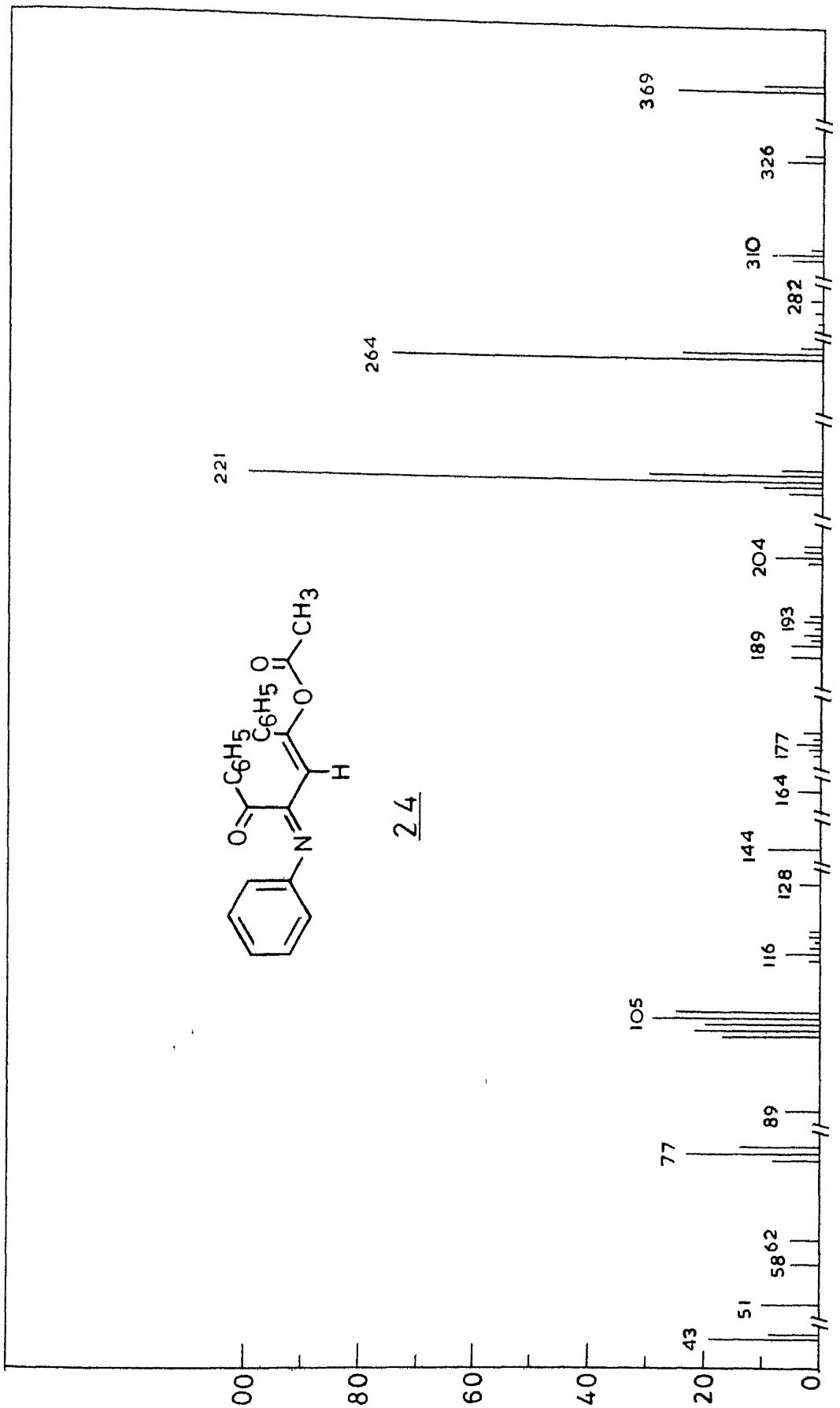
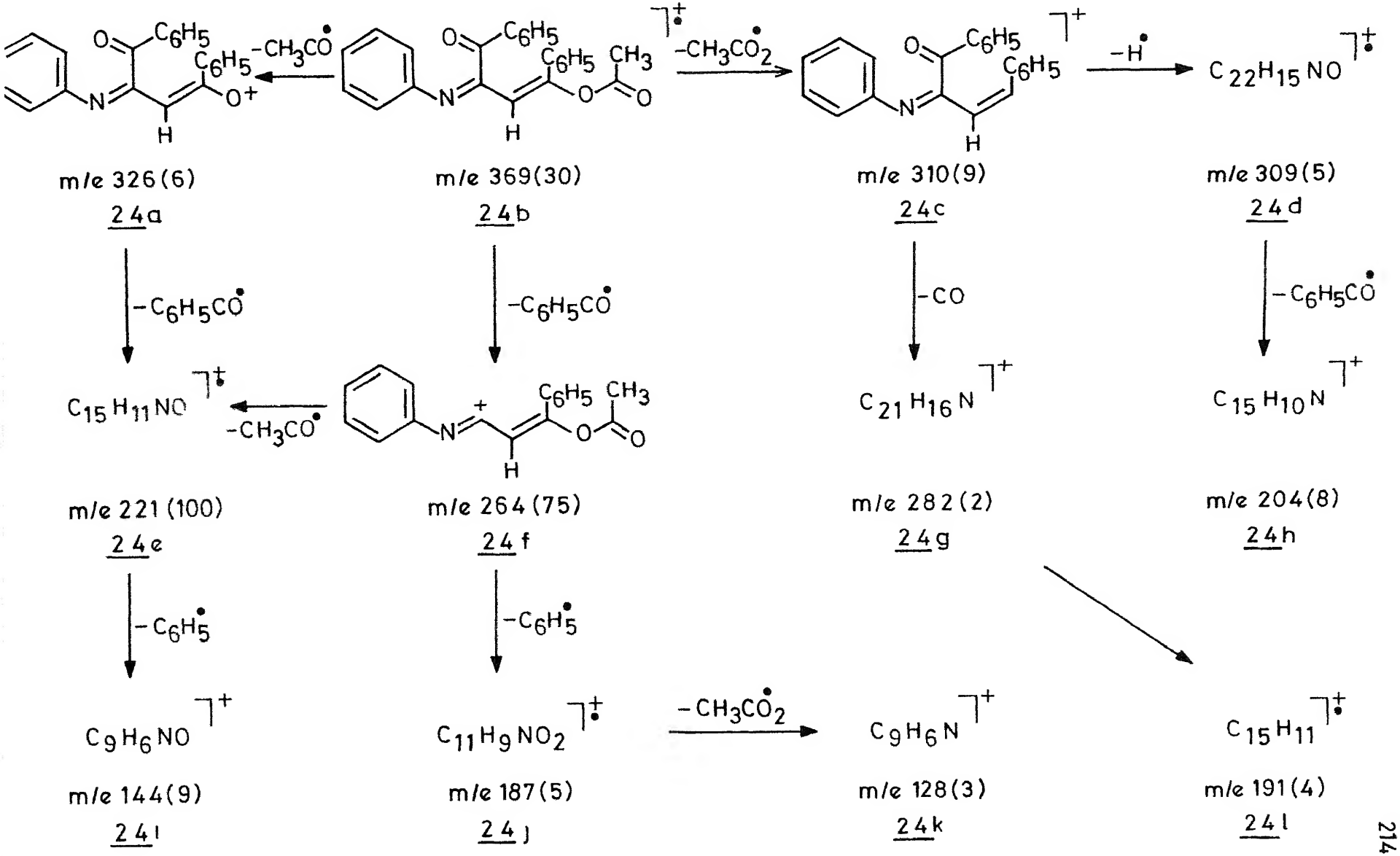


Fig IV.5 Mass spectrum of 24.

Scheme IV.6


m/e 326(6)
24a
m/e 369(30)
24b
m/e 310(9)
24c
m/e 309(5)
24d
m/e 221 (100)
24e
m/e 264 (75)
24f
m/e 282 (2)
24g
m/e 204(8)
24h
m/e 144(9)
24i
m/e 187(5)
24j
m/e 128(3)
24k
m/e 191(4)
24l

and benzoyl groups. The NMR spectrum of 25 (Fig. IV.6) showed a singlet at δ 2.30 (3 H), assigned to the methyl group, a one proton singlet at δ 6.30, assigned to the vinylic hydrogen and a complex multiplet centred around δ 7.48 (19 H), assigned to the aromatic hydrogens.

In the present studies, we have examined the photochemical transformations of the enol esters 23, 24 and 25, formed from the corresponding enamine diones, with a view to examining the type of photorearrangements they will undergo. Mention may be made in this connection that the phototransformations of a few enol esters are reported in the literature. In general, they are known to undergo α-cleavage, followed by acyl or aroyl group migrations, depending on the ester moieties.[11-14]

Irradiation of a solution of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23) in methanol in a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å), for example, resulted in the formation of a mixture of products, consisting of 1,4-diphenyl-4-methoxy-2-(N-phenylimino)but-3-en-1-one (27, 75%) and benzoic acid (65%) (Scheme IV.7). In a blank experiment, when the enol benzoate 23 was refluxed in methanol in dark for 3 hr, a 70% yield of 27 was obtained. Similarly, irradiation of the enol acetate 24 in methanol, under analogous conditions gave a 60% yield of the same product 27 (Scheme IV.7). In contrast, the irradiation of the enol benzoate

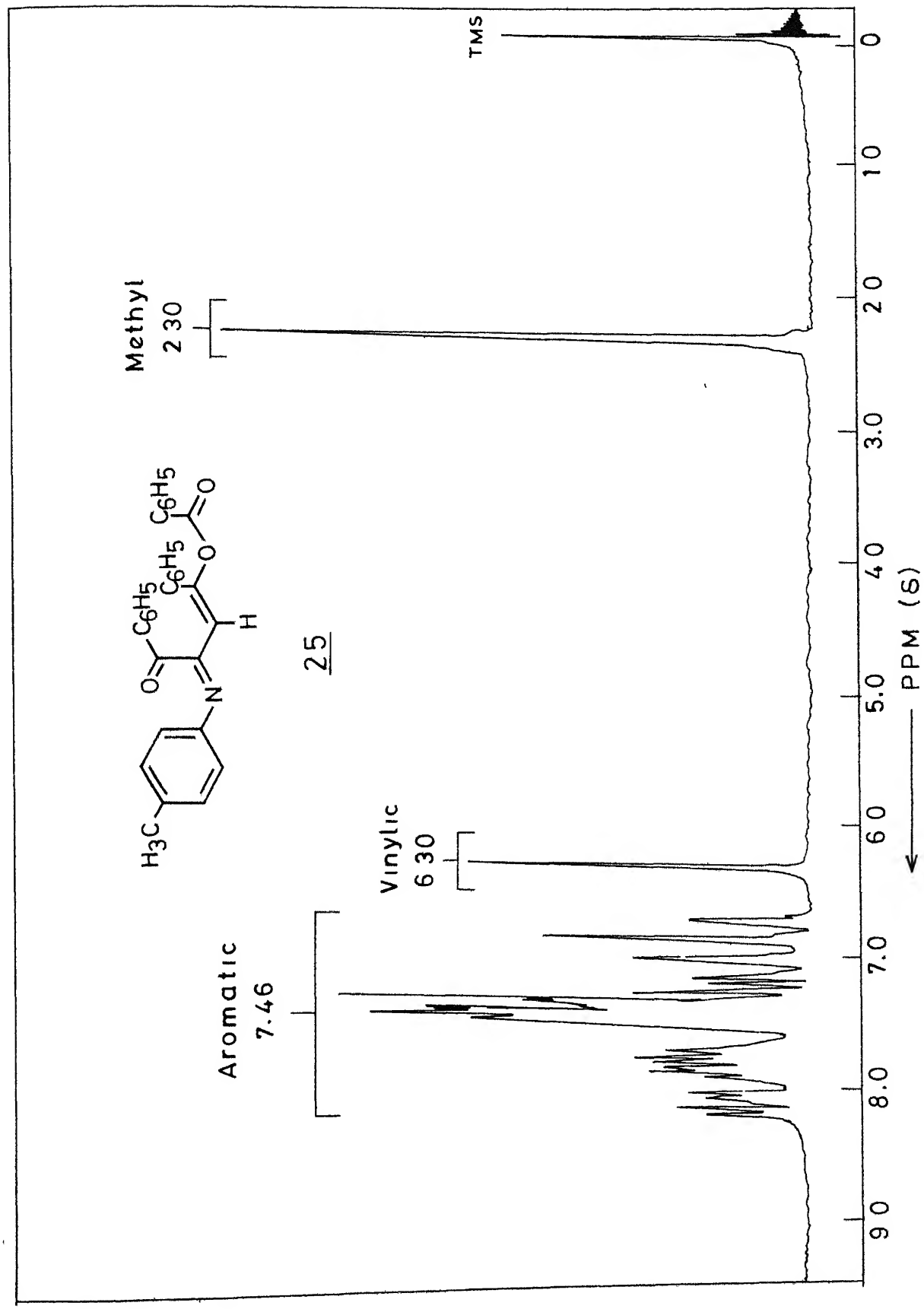
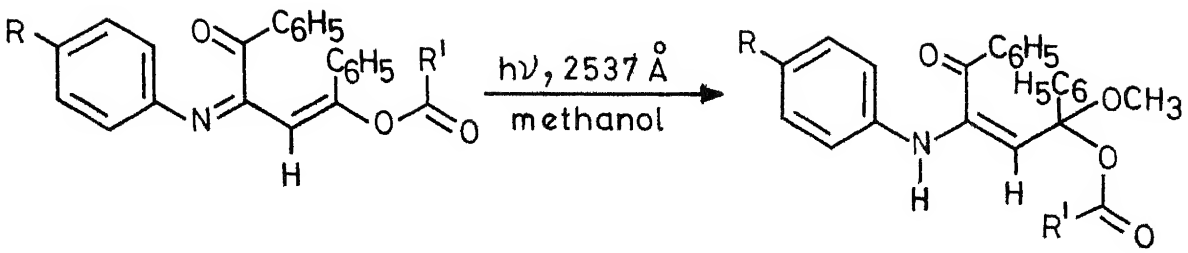


Fig. IV. 6 NMR spectrum (60 MHz) of 25

Scheme IV.7



23 , R = H ; R' = C_6H_5

24 , R = H ; R' = CH_3

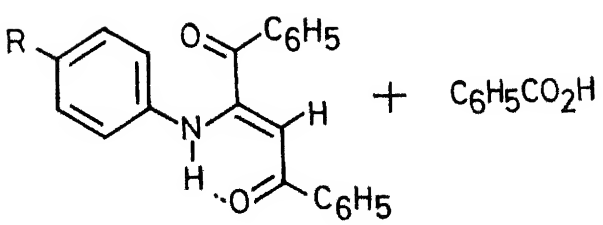
25 , R = CH_3 ; R' = C_6H_5

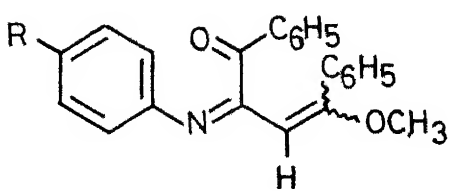
26 a , R = H , R' = C_6H_5

b , R = H , R' = CH_3

(c , R = CH_3 ; R' = C_6H_5)

$-R'CO_2H$





21 , R = CH_3

27 , R = H

(28 , R = CH_3)

25 in methanol using a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å) gave a 73% yield of the debenzoylated product 21 and benzoic acid (51%) (Scheme IV.7).

The structure of 27 was arrived at on the basis of analytical results and spectral data. The IR spectrum of 27 showed a carbonyl absorption at 1650 cm^{-1}. The NMR spectrum of 27 (Fig. IV.7) showed a singlet at δ 3.50 (3 H), assigned to the methoxy group and a one proton singlet at δ 6.08, assigned to the vinylic hydrogen. In addition, the spectrum consisted of a complex multiplet centred around δ 7.28 (15 H), assigned to the aromatic protons. Additional proof for the structure of 27 was obtained from its mass spectrum. The mass spectrum of 27 (Fig. IV.8) showed a molecular ion peak at m/e 341 (35). Other peaks in the spectrum were observed at m/e 326 (4), 310 (60), 236 (4), 221 (2), 220 (2), 206 (16), 205 (100), 204 (19), 191 (2), 165 (2), 144 (3), 137 (5), 128 (6), 116 (4), 105 (28), 103 (32), 77 (26) and 51 (30). Some of the probable fragmentation modes of 27 are shown in Scheme IV.8.

The formation of 27 in the photolysis of both 23 and 24 in methanol and also on treatment of 23 and 24 in refluxing methanol can be rationalized in terms of the pathways shown in Scheme IV.7. It is assumed that the addition of methanol to the enol benzoate 23, for example, will give rise to the adduct 26a, which in turn will lose elements of benzoic acid to give 27.

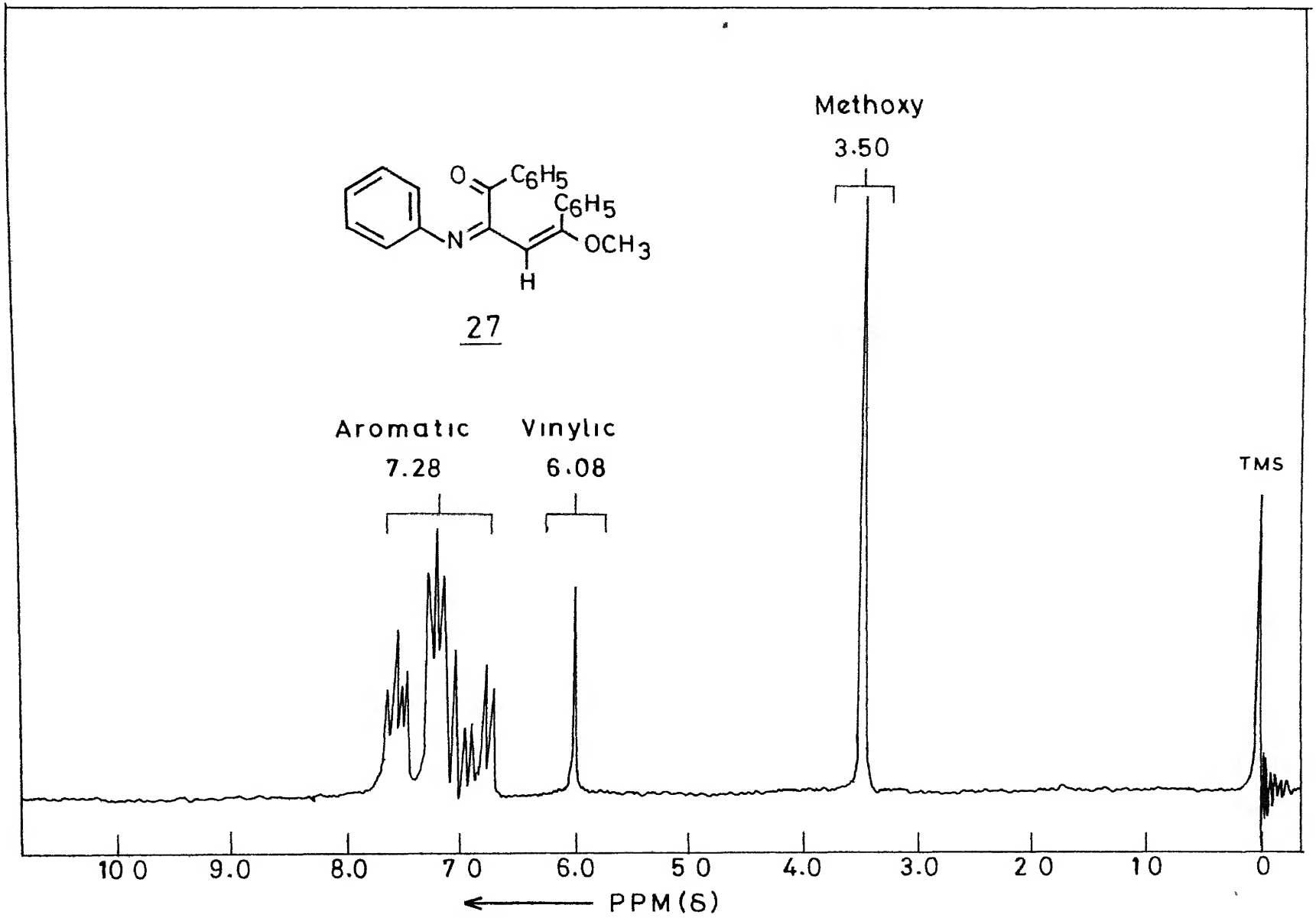


Fig. IV. 7 NMR spectrum (100 MHz) of 27.

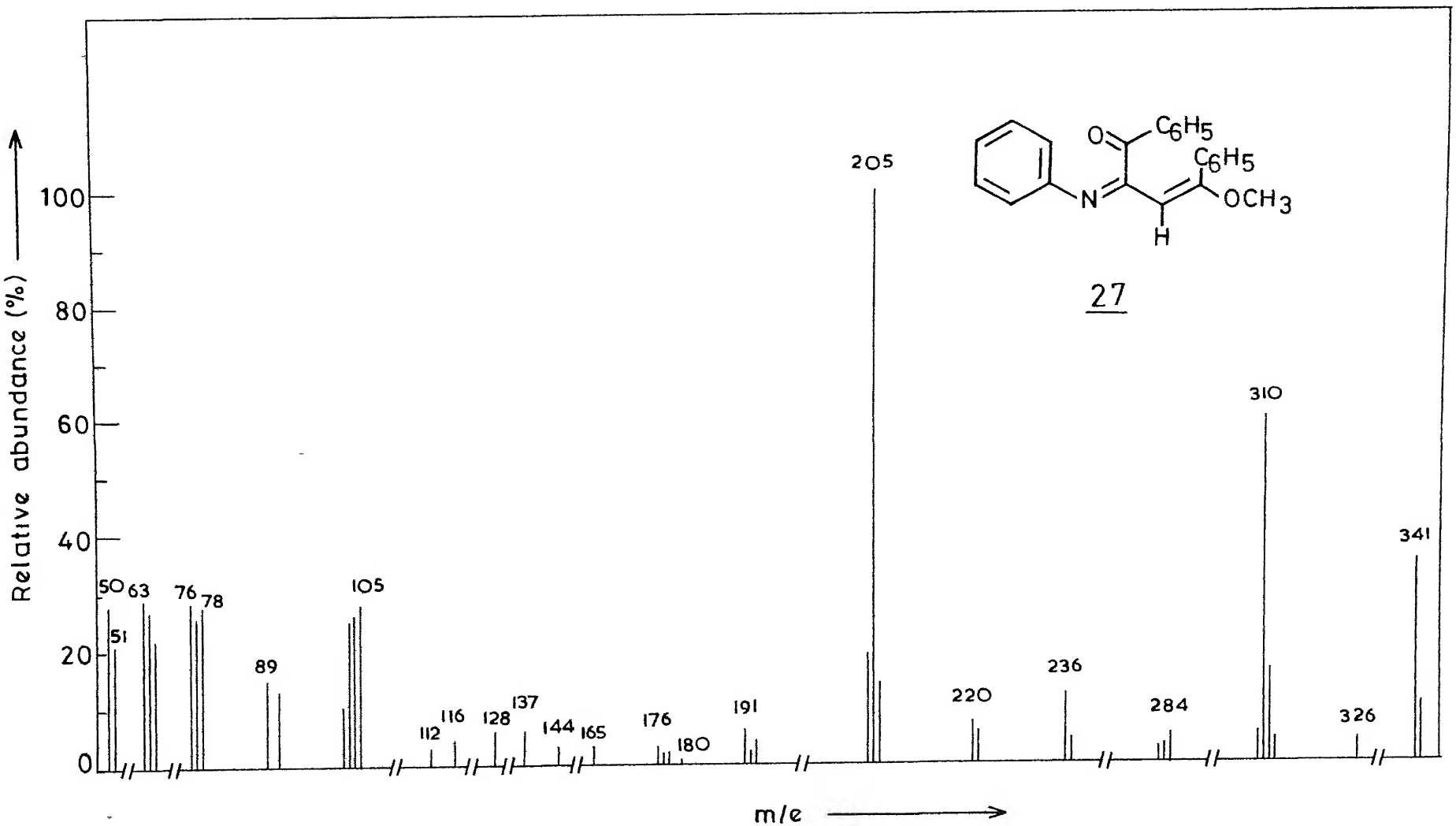
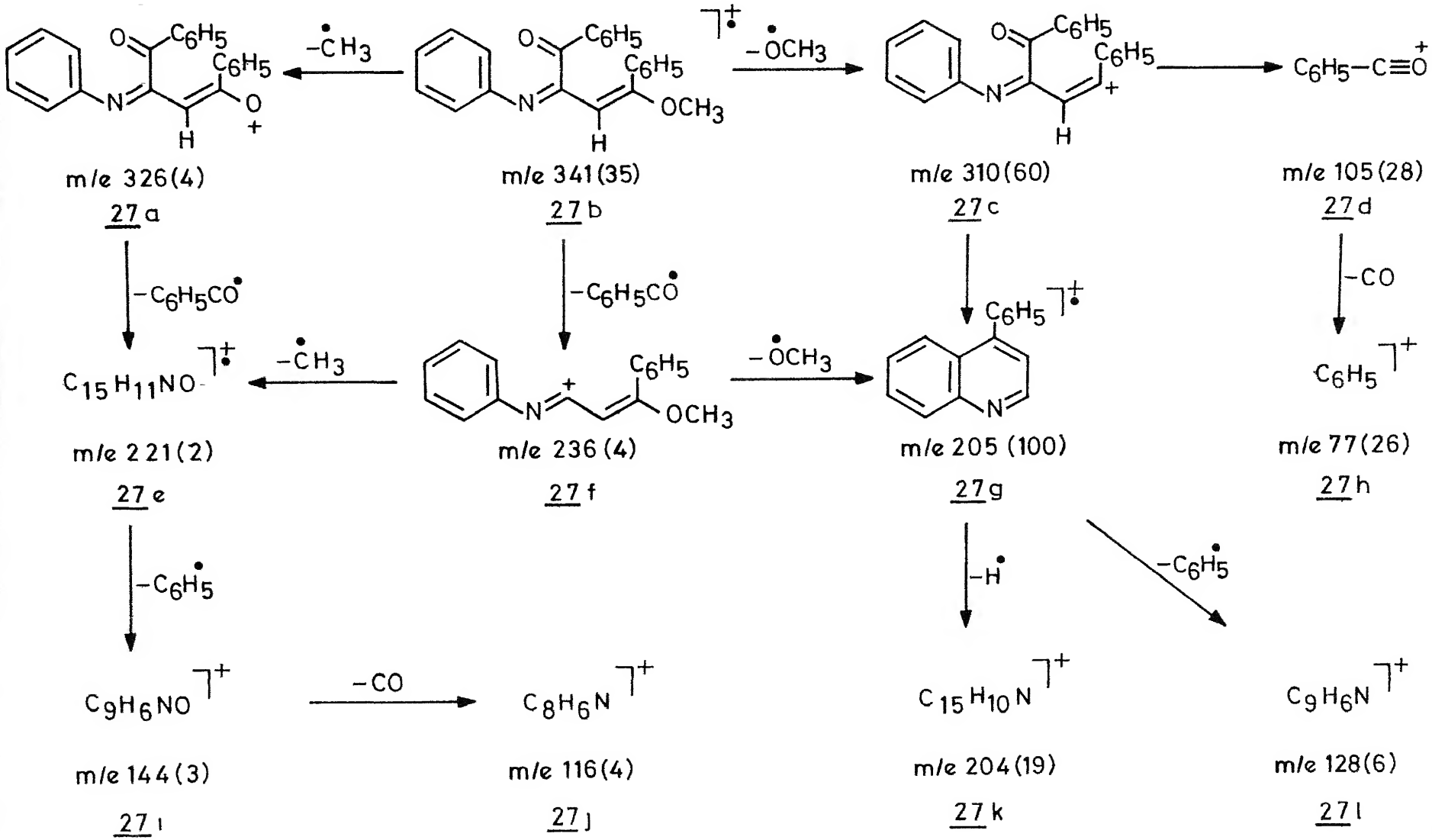


Fig IV. 8 Mass spectrum of 27

Scheme IV.8

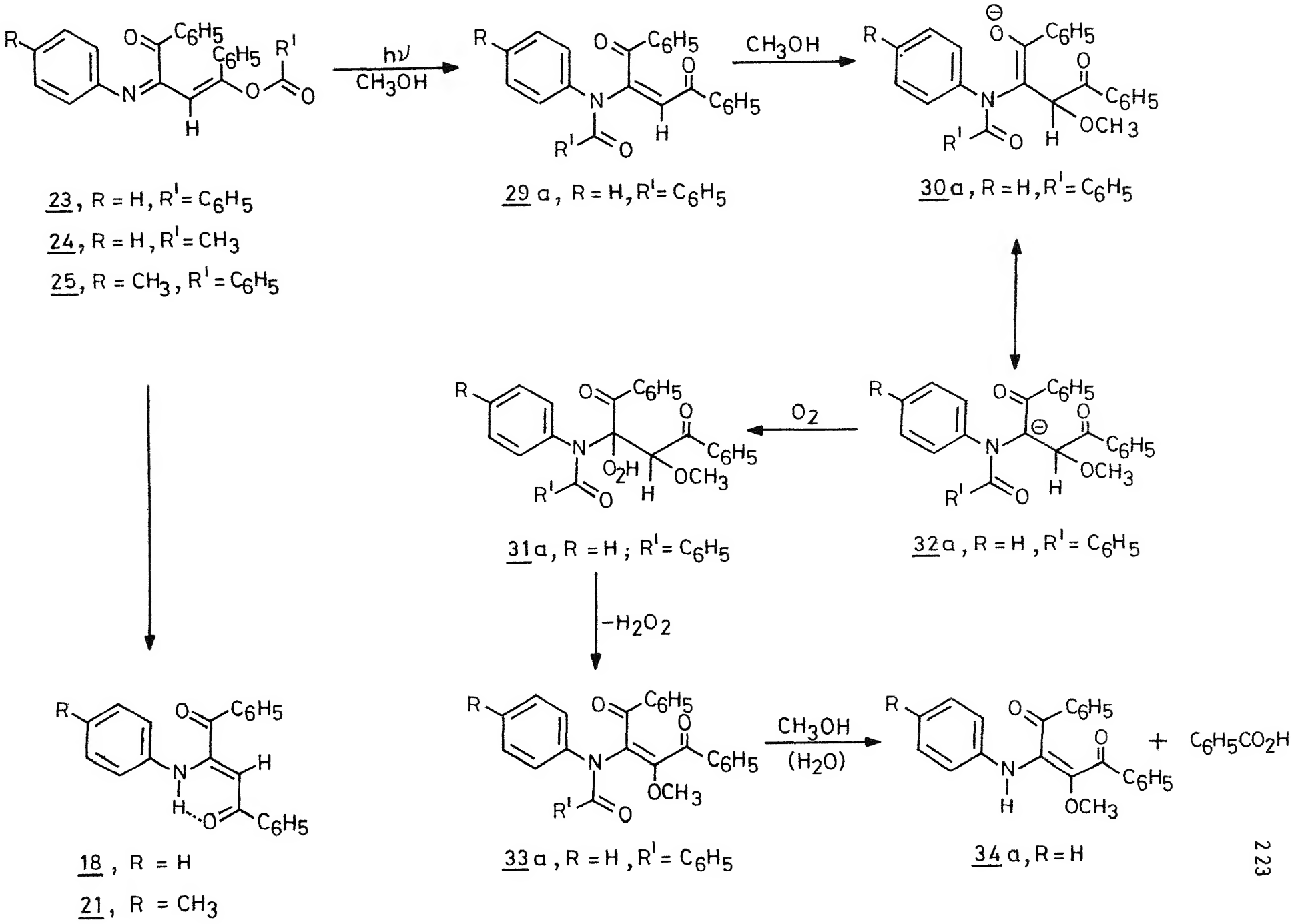

m/e 326(4)
27a
m/e 341(35)
27b
m/e 310(60)
27c
m/e 105(28)
27d
m/e 221(2)
27e
m/e 236(4)
27f
m/e 205(100)
27g
m/e 77(26)
27h
m/e 144(3)
27i
m/e 116(4)
27j
m/e 204(19)
27k
m/e 128(6)
27l

Similarly, the methanol adduct 26b formed from 24 will lose benzoic acid to give the same product 27, as shown in Scheme IV.7. It is not very clear why the irradiation of the enol benzoate 25 does not lead to the expected methoxy derivative 28. It appears that the major pathway under these conditions is a direct debenzoylation of 25, resulting in the formation of 21 and benzoic acid (Scheme IV.7).

When the irradiation of the enol benzoate 23 in methanol was carried using a 450-W Hanovia medium-pressure mercury lamp, a mixture of products consisting of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18, 40%), benzoic acid (50%) and 1,4-diphenyl-3-methoxy-2-(N-phenylamino)but-2-ene-1,4-dione (34a, 19%) was obtained (Scheme IV.9). However, the irradiation of a benzene solution of 23, employing a 450-W Hanovia medium-pressure mercury lamp, gave a mixture of 18 (61%) and benzoic acid (24%).

Similarly, the irradiation of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24) in methanol using a 450-W Hanovia medium-pressure mercury lamp gave a 34% yield of the deacetylated product, 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18). The irradiation of 24 in benzene, under analogous conditions, however, resulted in a 75% recovery of the unchanged starting material (24). Likewise, the irradiation of 4-benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one

Scheme IV 9



23, R = H, R' = C_6H_5

24, R = H, R' = CH_3

25, R = CH_3, R' = C_6H_5

29 a, R = H, R' = C_6H_5

30 a, R = H, R' = C_6H_5

32 a, R = H, R' = C_6H_5

31 a, R = H; R' = C_6H_5

33 a, R = H, R' = C_6H_5

34 a, R = H

18, R = H

21, R = CH_3

(25) in methanol, using a 450-W Hanovia medium-pressure mercury lamp gave a mixture of products consisting of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21, 76%) and benzoic acid (83%). None of the methoxy derivative, analogous to 34a, could be isolated from this reaction.

The structure of 34a was arrived at on the basis of analytical results and spectral data. The IR spectrum of 34a, for example, showed a free NH absorption at 3320 cm^{-1}, in addition to a carbonyl absorption at 1690 cm^{-1}. The NMR spectrum of 34a (Fig. IV.9) showed a singlet at δ 3.50 (3 H), assigned to the methoxy protons, another singlet at δ 5.15 (1 H, D_2O-exchangeable), assigned to the NH proton. In addition, the spectrum showed a complex multiplet centred around δ 7.11 (15 H) assigned to the aromatic protons. Further proof for the structure of 34a was derived from its mass spectrum. The mass spectrum of 34a (Fig. IV.10) showed an intense molecular ion peak at m/e 357 (50). Other peaks in the spectrum were observed at m/e 342 (1), 326 (2), 314 (1), 286 (1), 252 (100), 237 (15), 224 (3), 220 (2), 209 (3), 181 (2), 165 (10), 105 (25), 104 (18), 77 (25) and 51 (25). Some of the probable fragmentation modes of 34a are shown in Scheme IV.10.

The formation of 34a in the photolysis of 23 can be rationalized in terms of the pathway shown in Scheme IV.9. It has been assumed that the irradiation of 23 brings about an

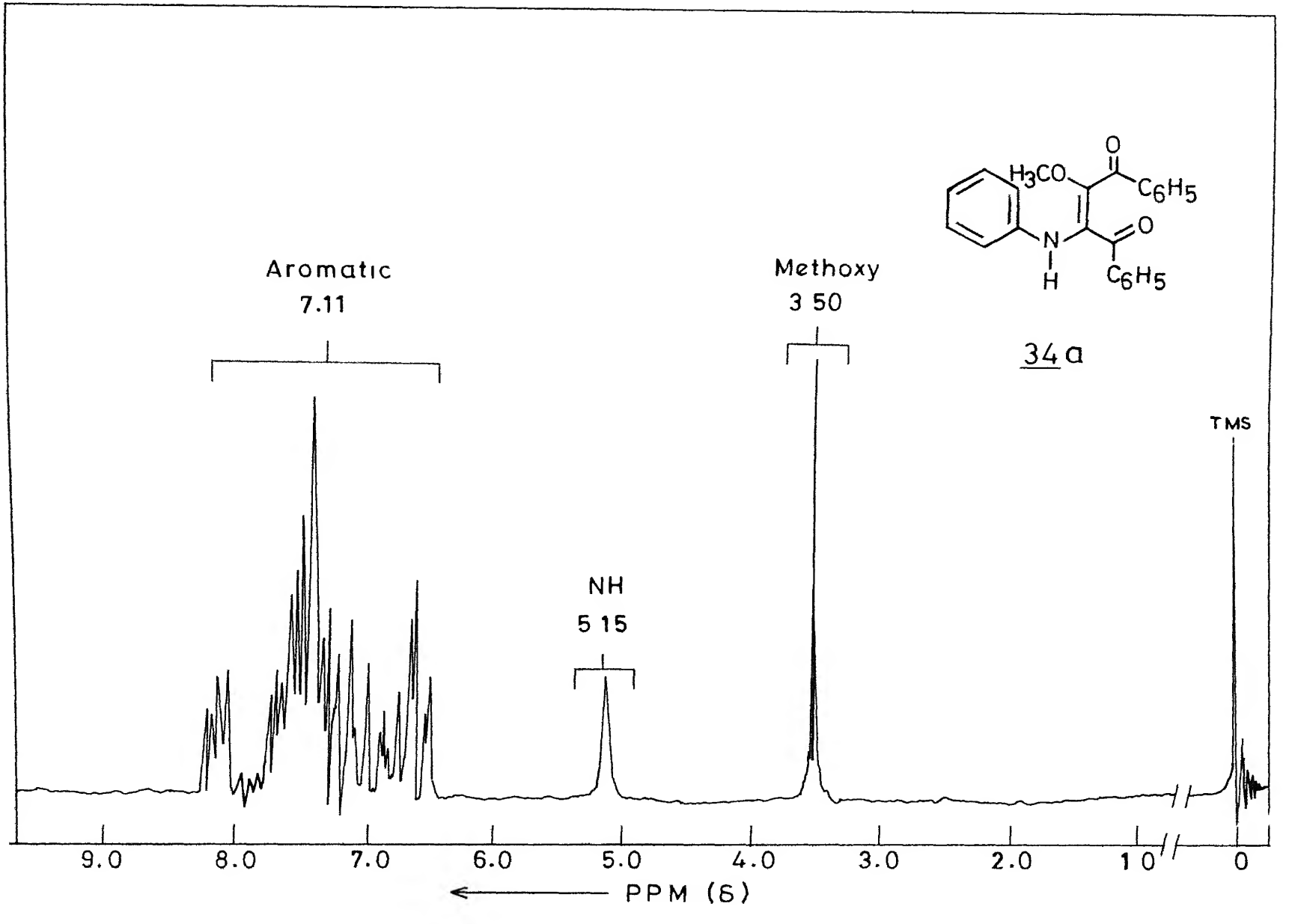


Fig. IV. 9 NMR spectrum (60 MHz) of 34 a.

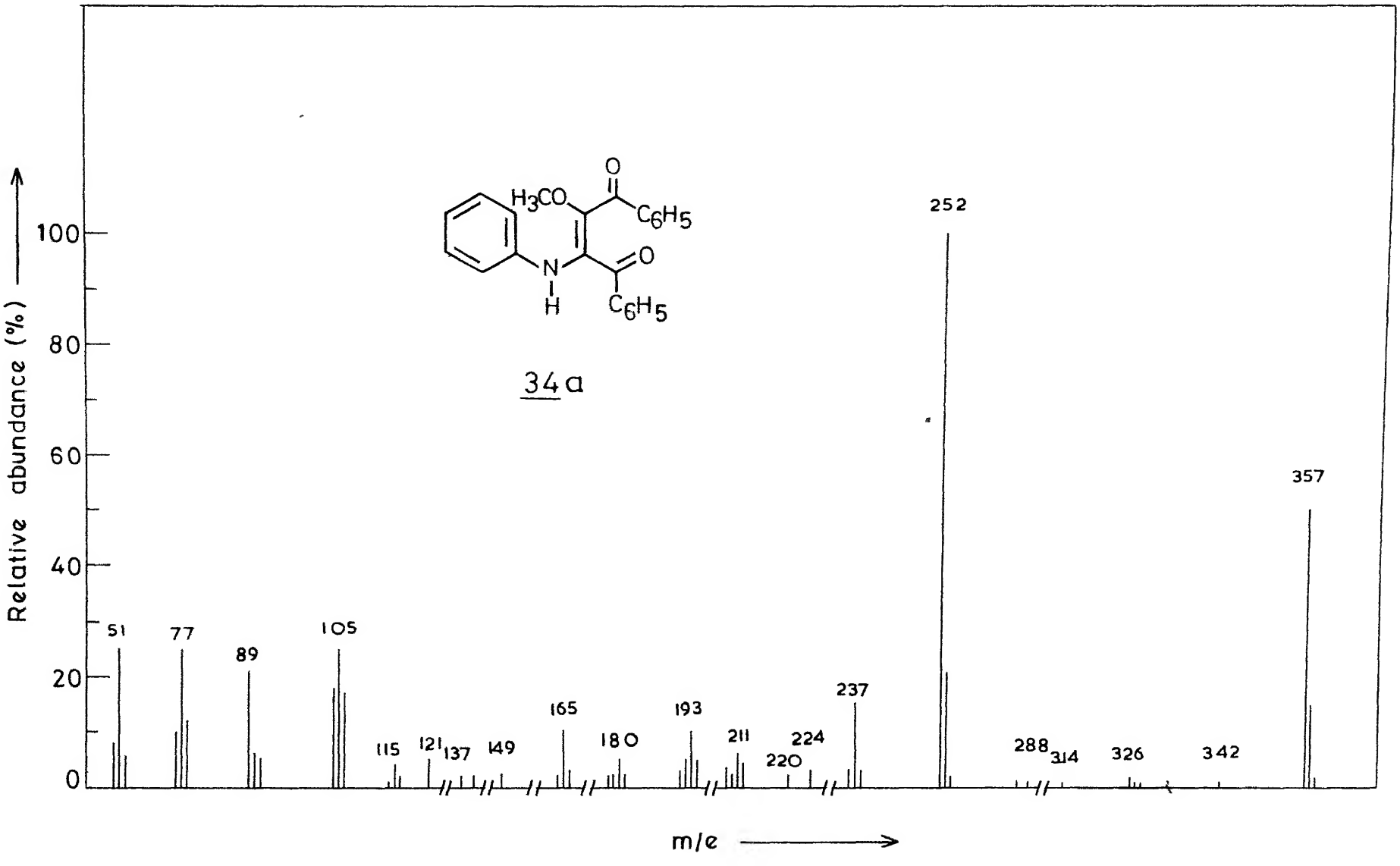
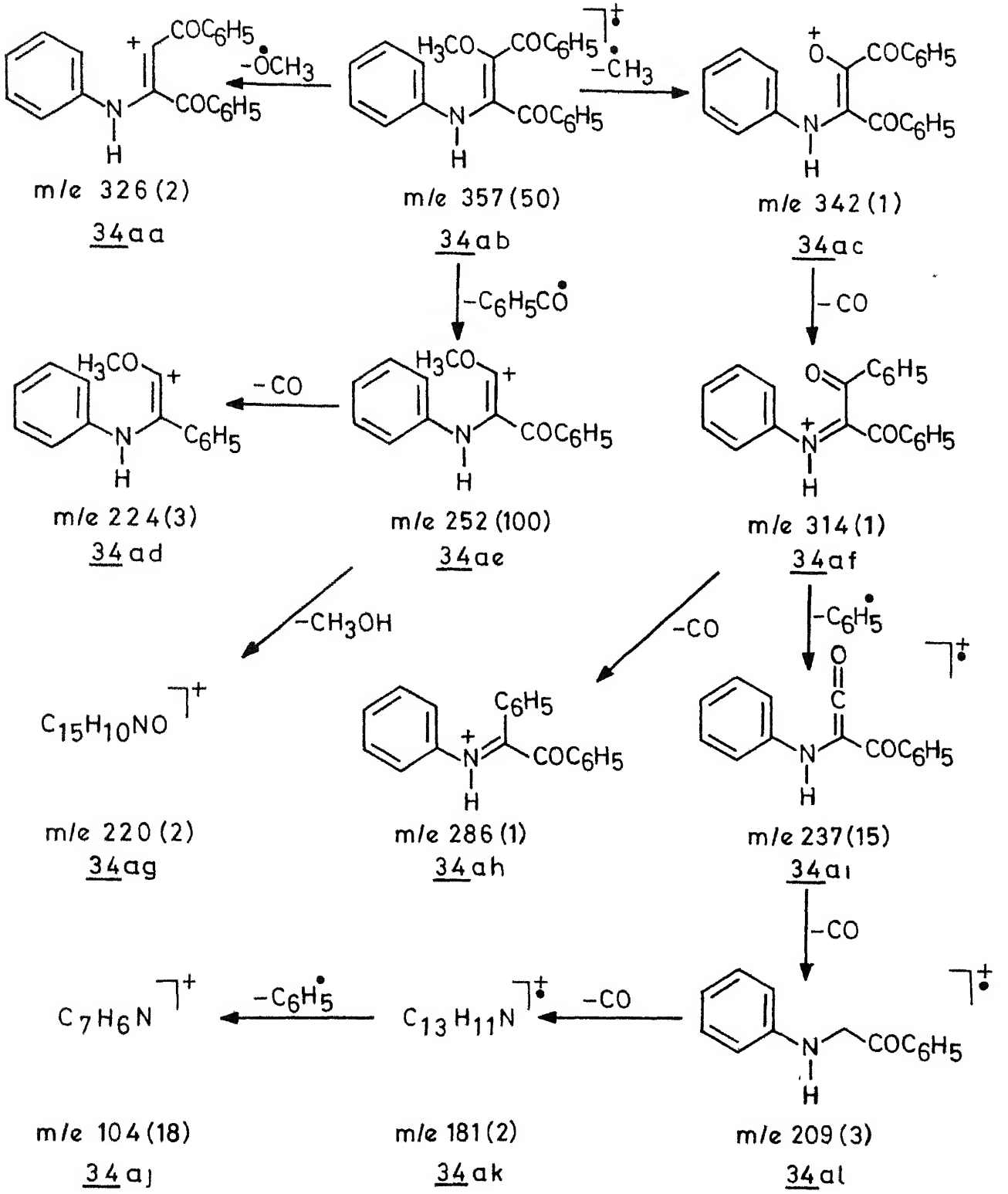


Fig IV.10 Mass spectrum of 34a.

Scheme IV.10

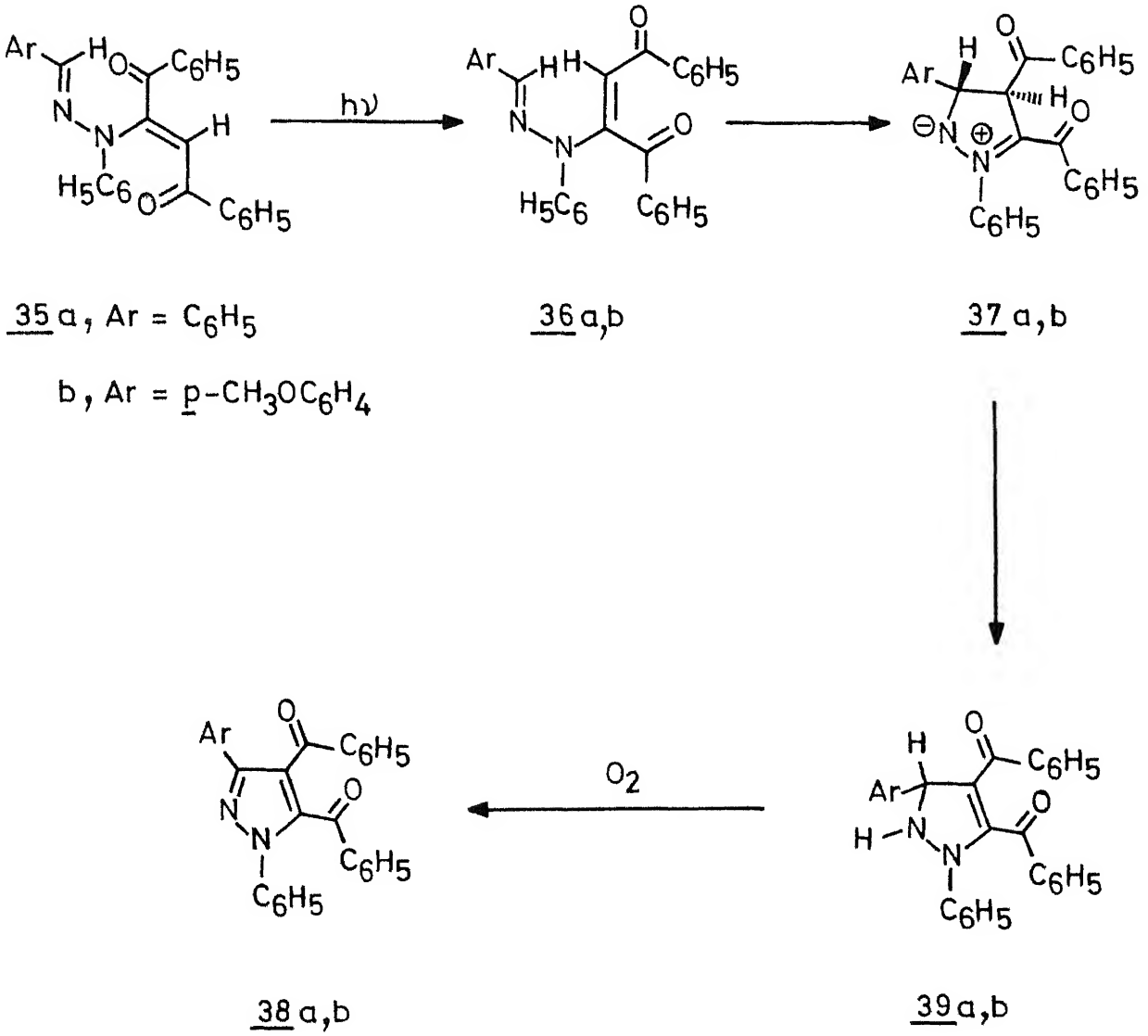

m/e 326 (2)
34aa
m/e 357 (50)
34ab
m/e 342 (1)
34ac
m/e 224 (3)
34ad
m/e 252 (100)
34ae
m/e 314 (1)
34af
C15H10NO
m/e 220 (2)
34ag
m/e 286 (1)
34ah
m/e 237 (15)
34ai
C7H6N
m/e 104 (18)
34aj
C13H11N
m/e 181 (2)
34ak
m/e 209 (3)
34al
-OCH3
-CH3
-C6H5CO
-CO
-CH3OH
-C6H5
-CO
-CO
-C6H5
-CO

initial benzoyl shift to give the N-benzoyl derivative 29a, which can subsequently undergo addition of methanol to give the intermediate 30a →32a. Subsequent oxygenation of 32a under the reaction conditions, followed by the loss of elements of hydrogen-peroxide will lead to the methoxy derivative 34a, as shown in Scheme IV.9. The formation of products such as 18 and 21 from 24 and 25, respectively, however, can be rationalized in terms of a simple debenzoylation reaction (Scheme IV.9).

In continuation of our studies, we have examined the photorearrangements of a few enehydrazine diones such as 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (35a) and 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (35b), formed from the reactions of benzaldehyde phenylhydrazone and p-anisaldehyde phenylhydrazone, respectively with DBA (see, Chapter II of this thesis).

Irradiation of a solution of 35a in methanol using a 450-W Hanovia medium-pressure mercury lamp for 2 hr resulted in the formation of a 63% yield of 4,5-dibenzoyl-1,3-diphenylpyrazole (38a). Similarly, irradiation of 35a, in benzene, under analogous conditions, gave a 77% yield of 38a. The irradiation of a methanol solution of 35b under analogous conditions, however, gave a 33% yield of a product identified as 3-(p-anisyl)-4,5-dibenzoyl-1-phenylpyrazole (38b) (Scheme IV.11).

Scheme IV.11



35 a, Ar = C_6H_5

b, Ar = p-$CH_3OC_6H_4$

36 a,b

37 a,b

39 a,b

38 a,b

The structure of 38b was arrived at on the basis of analytical results and spectral data. The IR spectrum of 38b, for example, showed a carbonyl absorption at 1660 cm^{-1}. The UV spectrum of 38b (Fig. IV.11) showed an absorption maximum at 256 nm (ε, 35,200) and was identical with the spectrum of 38a.

The formation of the pyrazoles 38a and 38b in the photo-transformations of 35a and 35b, respectively, can be rationalized in terms of the pathway shown in Scheme IV.11. It would be reasonable to assume that the irradiation of 35 leads to an initial cis-trans isomerization of the carbon-carbon double bond, resulting in the formation of 36a,b, which in turn can undergo conrotatory ring-closures of the pentadienyl anion-type,[15] leading to the zwitterionic intermediates 37a,b. Subsequent prototropic shifts will result in the formation of the pyrazolines 39a,b, which can undergo air-oxidation under the reaction conditions, resulting in the formation of the pyrazoles 38a,b (Scheme IV.11)

IV.4 EXPERIMENTAL

All melting points are uncorrected and were determined on a Mel-Temp melting-point apparatus. The IR spectra were recorded on Perkin-Elmer Model 377 or Model 580 infrared spectrometers. The electronic spectra were recorded on a Beckmann DB spectrophotometer or on a Cary 17-D spectrophotometer. The NMR

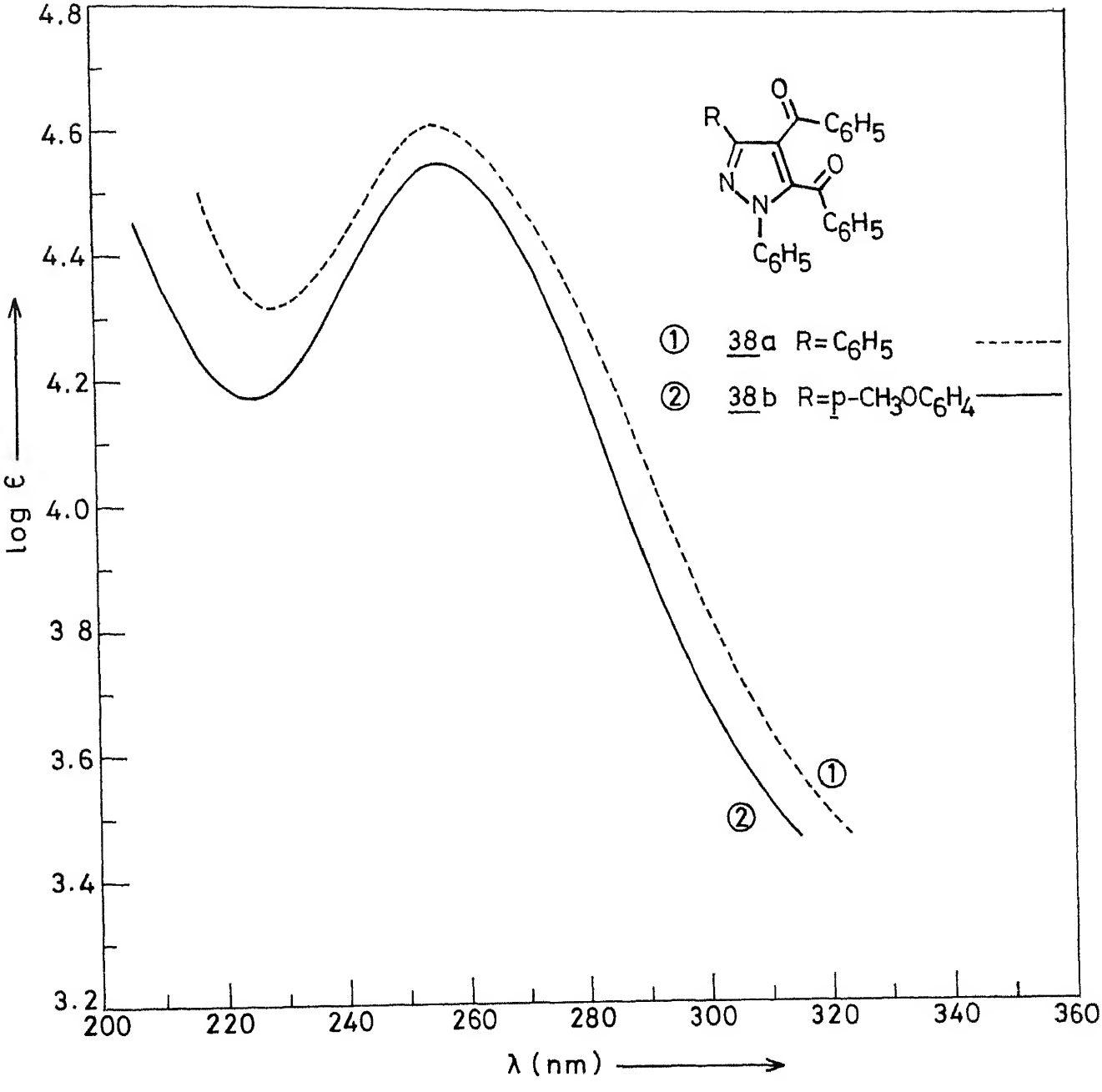


Fig. IV.11 UV spectra of 38a and 38b in methanol.

traces were recorded on a Varian HA-100, Varian A-60D or Jeol 100 MHz spectrometers, using tetramethylsilane (TMS) as internal standard. The mass spectra were recorded on á Hitachi RMU-6E single focussing mass spectrometer or a Varian Mat CH7 mass spectrometer at 70 eV. All the irradiation experiments were carried out either in a Srinivasan-Griffin Rayonet photochemical reactor (2537 Å or 3500 Å) or by using a Hanovia 450-W medium-pressure mercury lamp in a quartz-jacketed immersion well.

IV.4.1 Starting Materials

1,4-Diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18),[8] mp 130°, 1,4-diphenyl-2-(N-methyl-N-phenylamino)but-2-ene-1,4-dione (19),[9] mp 144-145°, 1,4-diphenyl-2-piperidinobut-2-ene-1,4-dione (20),[8] mp 179°, 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (35a),[10] mp 207°, 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (35b),[10] mp 209-210° and dibenzoylacetylene,[16] mp 111° were prepared by reported procedures. Solvents such as benzene and methanol were purified and dried by standard procedures. Petroleum ether used was the fraction, bp 60-80°.

IV.4.2 Irradiation of 1,4-Diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18) in Methanol

A Using a 2537 Å Light Source

A solution of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18, 0.11 g, 0.33 mmol) in methanol (150 ml) was irradiated for 40 hr, using a Srinivasan-Griffin Rayonet photochemical reactor. Removal of the solvent under vacuum gave a solid material, which was recrystallized from a mixture (3:1) of methanol and chloroform to give 90 mg (81%) of the unchanged starting material (18), mp 130° (mixture melting point)

B Using a Hanovia 450-W Medium-Pressure Mercury Lamp

A solution of 18 (0.327 g, 1 mmol) in methanol (250 ml) was irradiated for 4 hr. Work-up of the reaction mixture, as in the earlier case, gave 0.31 g (95%) of the unchanged starting material (18), mp 130° (mixture melting point), after recrystallization from a mixture (3:1) of methanol and chloroform.

IV.4.3 Irradiation of 1,4-Diphenyl-2-(N-methyl-N-phenylamino)but-2-ene-1,4-dione (19) in Methanol

A Using a 2537 Å Light Source

A solution of 1,4-diphenyl-2-(N-methyl-N-phenylamino)but-2-ene-1,4-dione (19, 0.17 g, 0.5 mmol) in methanol (250 ml) was irradiated for 30 hr, using a Srinivasan-Griffin Rayonet photochemical reactor. Work-up of the reaction mixture

as in earlier cases gave 0.155 g (91%) of the unchanged starting material (19), mp 144-145° (mixture melting point), after recrystallization from a mixture (3.1) of methanol and chloroform.

B Using a Hanovia 450-W Medium-Pressure Mercury Lamp

A solution of 19 (0.17 g, 0.5 mmol) in methanol (250 ml) was irradiated for 4 hr. Work-up of the reaction mixture as in the earlier cases gave 0.16 g (95%) of the unchanged starting material (19), mp 144-145° (mixture melting point), after recrystallization from a mixture (3:1) of methanol and chloroform.

IV.4.4 Irradiation of 1,4-Diphenyl-2-piperidino-but-2-ene-1,4-dione (20) in Methanol

A Using a 2537 Å Light Source

A solution of 1,4-diphenyl-2-piperidinobut-2-ene-1,4-dione (20, 0.106 g, 0.3 mmol) in methanol (100 ml) was irradiated for 10 hr. Removal of the solvent under vacuum gave 95 mg (90%) of the unchanged starting material (20), mp 179° (mixture melting point), after recrystallization from a mixture (2:1) of methanol and chloroform.

B Using a 3500 Å Light Source

A solution of 20 (0.106 g, 0.3 mmol) in methanol (100 ml) was irradiated for 10 hr using a Srinivasan-Griffin Rayonet photochemical reactor. Work-up of the reaction mixture as in

the earlier cases gave 90 mg (85%) of the unchanged starting material (20), mp 179° (mixture melting point), after recrystallization from a mixture (2:1) of methanol and chloroform.

IV.4.5 Preparation of 4-Benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23)

To a solution of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18, 0.98 g, 3 mmol) in pyridine (15 ml) was added benzoyl chloride (0.5 g, 3.5 mmol) dropwise, over a period of ½ hr. The reaction mixture was heated around 50-60° for ½ hr, cooled and subsequently neutralized with the requisite amount of hydrochloric acid. The mixture was extracted with benzene and the benzene-extract was washed several times with water and dried over anhydrous sodium sulfate. Removal of the solvent under vacuum gave a sticky mass, which solidified on treatment with a small amount of methanol. Recrystallization of this product from a mixture (2:1) of benzene and petroleum ether gave 1.0 g (78%) of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23), mp 170-171°.

Anal. Calcd for $C_{29}H_{21}NO_3$. C, 80.74; H, 4.87; N, 3.24; Mol. wt., 431. Found: C, 80.33; H, 4.96; N, 3.40; Mol. wt., 431 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}, aromatic), 1740 ($\nu_{C=O}$, ester), 1655 ($\nu_{C=O}$, keto), 1608 ($\nu_{C=N}$), 1585, 1570 and 1490 ($\nu_{C=C}$) and 1265 cm^{-1} (ν_{C-O-C}).

UV spectrum (methanol) λ_{max}: 235 nm (ε, 25,900), 320 (14,900) and 355 (12,000, sh).

IV.4.6 Preparation of 4-Acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24)

Acetyl chloride (1.17 g, 0.015 mol) was added dropwise to a well-stirred solution of 1,4-diphenyl-2-(N-phenylamino)-but-2-ene-1,4-dione (18, 3.27 g, 0.01 mol) in pyridine (25 ml) at 0°C, over a period of ½ hr. The reaction mixture was stirred at room temperature for an additional period of 2 hr and was then treated with water and subsequently neutralized with the requisite amount of hydrochloric acid. The organic material was extracted with benzene and the benzene-extract was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a product, which was recrystallized from ethanol to give 2.8 g (76%) of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24), mp 148-149°.

Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.05; H, 5.15; N, 3.79; Mol. wt., 369. Found: C, 78.21; H, 5.10; N, 3.42; Mol. wt., 369 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}, aromatic), 2930 and 2850 (ν_{C-H}, asymmetric and symmetric), 1760 ($\nu_{C=O}$, ester), 1660 ($\nu_{C=O}$, keto), 1610 ($\nu_{C=N}$), 1590, 1570 and 1490 ($\nu_{C=C}$) and 1210 cm^{-1} (ν_{C-O-C}).

UV spectrum (methanol) λ_{max}: 255 nm (ε, 20,600), 320 (12,200, sh) and 365 (17,100).

IV.4.7 Preparation of 1,4-Diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21)

A mixture of p-toluidine (2.14 g, 0.02 mol) and DBA (4.68 g, 0.02 mol) in THF (50 ml) was refluxed for 1 hr. Removal of the solvent under reduced pressure gave a product, which was recrystallized from a mixture (2:1) of methanol and chloroform to give 4.5 g (67%) of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21), mp 158°.

Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.93; H, 5.57; N, 4.11; Found: C, 80.60; H, 5.80; N, 4.39.

IR spectrum (KBr) ν_{max}: 3180 (ν_{N-H}, intramolecularly hydrogen-bonded), 3060 and 3040 (ν_{C-H}, aromatic), 2920 and 2860 (ν_{C-H}, asymmetric and symmetric), 1670 ($\nu_{C=O}$), 1590, 1570 and 1550 ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 255 nm (ε, 21,300) and 370 (17,000).

IV.4.8 Preparation of 4-Benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one (25)

Benzoyl chloride (1.96 g, 0.04 mol) was added dropwise to a well-stirred solution of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21, 4.54 g, 0.013 mol) in pyridine (50 ml), at room temperature. The reaction mixture was heated around 50-60° for ½ hr, cooled and then neutralized with the necessary amount of hydrochloric acid. The mixture was extracted with benzene and the benzene-extract was worked up as in the earlier cases to give 3.54 g (60%) of 4-benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one (25), mp 108°, after recrystallization from a mixture (1:1) of benzene and petroleum ether.

Anal. Calcd for $C_{30}H_{23}NO_3$: C, 80.89; H, 5.17; N, 3.14; Found: C, 81.06; H, 4.88; N, 2.79.

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}, aromatic), 2920 and 2860 (ν_{C-H}, asymmetric and symmetric), 1740 ($\nu_{C=O}$, ester), 1650 ($\nu_{C=O}$, keto), 1610 ($\nu_{C=N}$), 1595, 1570 and 1500 ($\nu_{C=C}$) and 1265 cm^{-1} (ν_{C-O-C}).

UV spectrum (methanol) λ_{max}: 236 nm (ε, 30,500), 314 (17,700) and 354 (13,400, sh).

IV.4.9 Irradiation of 4-Benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23) in Methanol Using a 2537 Å Light Source

A solution of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23, 0.431 g, 1 mmol) in methanol (175 ml)

was irradiated for 20 hr using a Srinivasan-Griffin Rayonet photochemical reactor. Removal of the solvent under reduced pressure gave a residue, which was treated with a 5% solution of sodium bicarbonate. The bicarbonate extract was acidified with dilute hydrochloric acid to give 80 mg (65%) of benzoic acid, mp 122° (mixture melting point), after recrystallization from a mixture (1:9) of benzene and petroleum ether.

The material that was left behind after the bicarbonate treatment was extracted with methylene chloride (50 ml) and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a solid, which was recrystallized from ethanol to give 0.25 g (75%) of 1,4-diphenyl-4-methoxy-2-(N-phenylimino)but-3-en-1-one (27), mp 125-126°.

Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.93; H, 5.57; N, 4.10; Mol. wt., 341. Found: C, 80.72; H, 5.20; N, 4.02; Mol. wt., 341 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3045 (ν_{C-H}, aromatic), 2960 and 2880 (ν_{C-H}, asymmetric and symmetric), 1650 ($\nu_{C=O}$), 1600 ($\nu_{C=N}$), 1580, 1560 and 1480 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 240 nm (ε, 10,700), 324 (12,500) and 350 (10,900, sh).

IV.4.10 Methanolysis of 4-Benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23)

A solution of 23 (0.431 g, 1 mmol) in methanol (25 ml) was refluxed for 3 hr in the dark. Removal of the solvent under reduced pressure and work-up of the resultant product, as in the earlier case, gave 75 mg (61%) of benzoic acid, mp 122° (mixture melting point) and 0.24 g (70%) of 1,4-diphenyl-4-methoxy-2-(N-phenylimino)but-3-en-1-one (27), mp 125-126° (mixture melting point).

IV.4.11 Irradiation of 4-Acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24) in Methanol Using a 2537 Å Light Source

A solution of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24, 0.369 g, 1 mmol) in methanol (175 ml) was irradiated for 15 hr using a Srinivasan-Griffin Rayonet photochemical reactor. Removal of the solvent under vacuum gave a product which was recrystallized from ethanol to give 0.205 g (60%) of 1,4-diphenyl-4-methoxy-2-(N-phenylimino)but-3-en-1-one (27), mp 125-126° (mixture melting point).

IV.4.12 Methanolysis of 4-Acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24)

A solution of 24 (0.369 g, 1 mmol) in methanol (25 ml) was refluxed for 3 hr in the dark. Removal of the solvent under reduced pressure gave 0.24 g (70%) of 27, mp 125-126° (mixture melting point), after recrystallization from ethanol.

IV.4.13 Irradiation of 4-Benzoyloxy-1,4-diphenyl-2-(N-p-tolylamino)but-3-en-1-one (25) in Methanol Using a 2537 Å Light Source

A solution of 4-benzoyloxy-1,4-diphenyl-2-(N-phenylamino)but-3-en-1-one (25, 0.25 g, 0.56 mmol) in methanol (250 ml) was irradiated for 6 hr, using a Srinivasan-Griffin Rayonet photochemical reactor. Work-up of the reaction mixture as in the earlier cases, gave 35 mg (51%) of benzoic acid, mp 122° (mixture melting point) and 0.14 g (73%) of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21), mp 158° (mixture melting point).

IV.4.14 Irradiation of 4-Benzoyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (23) Using a Hanovia Medium-Pressure Mercury Lamp

A In Methanol

A solution of 23 (0.645 g, 1.5 mmol) in methanol (700 ml) was irradiated for 3 hr. The irradiation was repeated to photolyse in all 1.29 g (3 mmol) of 23. Removal of the solvent under reduced pressure gave a residual solid, which was treated with aqueous sodium bicarbonate (5%). The aqueous layer, on acidification with dilute hydrochloric acid and work-up in the usual manner, gave 0.18 g (50%) of benzoic acid, mp 122° (mixture melting point), after recrystallization from a mixture (1:9) of benzene and petroleum ether.

The material that was left behind after extraction with bicarbonate was chromatographed over silica gel. Elution with a mixture (3:7) of benzene and petroleum ether gave 0.4 g (40%) of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18), mp 130° (mixture melting point), after recrystallization from a mixture (3:1) of methanol and chloroform

Further elution of the column with a mixture (1:1) of benzene and petroleum ether gave 0.22 g of an unidentified product, mp 195°.

Anal. Found: C, 79.78; H, 5.34; N, 6.30

IR spectrum (KBr) ν_{max}: 3330, 3060 (ν_{C-H}, aromatic), 1605, 1585 and 1530 ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 248 nm (ε, 36,800) and 285 (20,700).

NMR spectrum ($CDCl_3$): δ 7.15 (m, aromatic).

Mass spectrum m/e (relative intensity): 414 (M^+) (100), 386 (1), 337 (7), 309 (7), 232 (6), 231 (6), 217 (6), 204 (17), 180 (14), 168 (9), 165 (6), 131 (6), 108 (26), 105 (27), 80 (21), 77 (4) and 53 (6).

Continued elution of the column with benzene gave 0.2 g (19%) of 1,4-diphenyl-3-methoxy-2-(N-phenylamino)but-2-ene-1,4-dione (34a), mp 184°, after recrystallization from a mixture (2:1) of benzene and petroleum ether.

Anal. Calcd for $C_{23}H_{19}NO_3$: C, 77.81; H, 5.32; N, 3.92; Mol. wt., 357. Found: C, 77.90; H, 5.21; N, 4.34; Mol. wt., 357 (Mass spectrometry).

IR spectrum (KBr) ν_{max}: 3320 (ν_{N-H}), 3040 (ν_{C-H}, aromatic), 2930 and 2860 (ν_{C-H}, asymmetric and symmetric), 1690 ($\nu_{C=O}$), 1605, 1590 and 1565 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 245 nm (ε, 25,400), 304 (17,100), 325 (14,900, sh) and 435 (1,800)

B In Benzene

A solution of 23 (0.215 g, 0.5 mmol) in benzene (250 ml) was irradiated for 3 hr, using a Hanovia 450-W medium-pressure mercury lamp. The irradiation was repeated a few times to photolyse in all, 0.86 g (2 mmol) of 23. Removal of the solvent under reduced pressure from the combined photolysates gave a product which was treated with a 5% solution of aqueous sodium bicarbonate. Acidification of the bicarbonate extract with dilute hydrochloric acid gave 60 mg (24%) of benzoic acid, mp 122° (mixture melting point), after recrystallization from a mixture (1:9) of benzene and petroleum ether.

The material that was left behind after extraction with bicarbonate was chromatographed over silica gel. Elution with a mixture (1:9) of benzene and petroleum ether gave a product, which was recrystallized from a mixture (3:1) of

methanol and chloroform, to give 0.4 g (61%) of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18), mp 130° (mixture melting point).

Further elution of the column with a mixture (3:7) of benzene and petroleum ether gave 0.2 g (23%) of the unchanged starting material (23), mp 170-171° (mixture melting point).

Subsequent elution of the column with a mixture (1:1) of benzene and petroleum ether gave 0.1 g of the unidentified product, mp 195° (mixture melting point).

IV.4.15 Irradiation of 4-Acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24)

A In Methanol

A solution of 4-acetyloxy-1,4-diphenyl-2-(N-phenylimino)but-3-en-1-one (24, 0.44 g, 1.2 mmol) in methanol (700 ml) was irradiated for 3 hr, using a Hanovia 450-W medium-pressure mercury lamp. The experiment was repeated a few times to photolyse, in all, 1.32 g (3.6 mmol) of 24. Removal of the solvent under vacuum gave a residue, which was chromatographed over silica gel. Elution with a mixture (1:1) of benzene and petroleum ether gave 0.4 g (34%) of 1,4-diphenyl-2-(N-phenylamino)but-2-ene-1,4-dione (18), mp 130° (mixture melting point), after recrystallization from a mixture (2:1) of methanol and chloroform.

Further elution with a mixture (3:1) of benzene and petroleum ether gave a solid, which was recrystallized from a mixture (2:1) of benzene and petroleum ether to give 0.2 g of the unidentified product, mp 195° (mixture melting point).

B In Benzene

A solution of 24 (0.185 g, 0.5 mmol) in benzene (250 ml) was irradiated for 4 hr using a Hanovia 450-W medium-pressure mercury lamp. Removal of the solvent under vacuum and work-up of the resultant residue gave 0.155 g (75%) of the unchanged starting material (24), mp 148-149° (mixture melting point).

IV.4.16 Irradiation of 4-Benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one (25) in Methanol

A solution of 4-benzoyloxy-1,4-diphenyl-2-(N-p-tolylimino)but-3-en-1-one (25, 0.665 g, 1 mmol) in methanol (700 ml) was irradiated for 3 hr, using a Hanovia 450-W medium-pressure mercury lamp. Removal of the solvent under vacuum gave a residue, which was treated with a 5% solution of sodium bicarbonate. Acidification of the bicarbonate extract with dilute hydrochloric acid gave 0.15 g (83%) of benzoic acid, mp 122° (mixture melting point), after recrystallization from a mixture (1:9) of benzene and petroleum ether.

The material that was left behind after bicarbonate treatment was chromatographed over silica gel. Elution with a mixture (3:7) of benzene and petroleum ether gave 0.39 g (76%) of 1,4-diphenyl-2-(N-p-tolylamino)but-2-ene-1,4-dione (21), mp 158° (mixture melting point), after recrystallization from a mixture (2:1) of benzene and petroleum ether.

IV.4.17 Irradiation of 2-(1'-Phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (35a)

A In Methanol

A solution of 2-(1'-phenylhydrazinyl-2'-benzylidene)-1,4-diphenylbut-2-ene-1,4-dione (35a, 0.8 g, 1.85 mmol) in methanol (600 ml) was irradiated for 2 hr, using a Hanovia 450-W medium-pressure mercury lamp. Removal of the solvent under reduced pressure gave a solid, which was recrystallized from methanol to give 0.5 g (63%) of 4,5-dibenzoyl-1,3-diphenylpyrazole (38a), mp 136-137° (lit.[17] mp 136-137°).

Anal. Calcd for $C_{29}H_{20}N_2O_2$: C, 81.32; H, 4.67; N, 6.54. Found: C, 81.75; H, 4.65; N, 6.57.

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}, aromatic), 1660 ($\nu_{C=O}$), 1645 ($\nu_{C=N}$), 1598, 1580 and 1500 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 255 nm (ε, 39,700).

B In Benzene

A solution of 35a (0.3 g, 0.7 mmol) in benzene (175 ml) was irradiated for 2 hr, using a Hanovia 450-W medium-pressure mercury lamp. Removal of the solvent under vacuum gave a product, which was recrystallized from methanol to give 0.23 g (77%) of 4,5-dibenzoyl-1,3-diphenylpyrazole (38a), mp 136-137° (mixture melting point).

IV.4.18 Irradiation of 2-(1'-Phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (35b) in Methanol

A solution of 2-(1'-phenylhydrazinyl-2'-(p-methoxybenzylidene))-1,4-diphenylbut-2-ene-1,4-dione (35b, 0.23 g, 0.5 mmol) in methanol (700 ml) was irradiated for 10 hr, using a Hanovia 450-W medium-pressure mercury lamp. Removal of the solvent under reduced pressure gave a product, which was chromatographed over silica gel. Elution with benzene gave 75 mg (33%) of 3-(p-anisyl)-4,5-dibenzoyl-1-phenylpyrazole (38b), mp 133°, after recrystallization from methanol.

Anal. Calcd for $C_{30}H_{22}N_2O_3$: C, 78.59; H, 4.80; N, 6.11. Found: C, 78.96; H, 4.80; N, 5.92.

IR spectrum (KBr) ν_{max}: 3060 (ν_{C-H}, aromatic), 2930 and 2840 (ν_{C-H}, asymmetric and symmetric), 1660 ($\nu_{C=O}$), 1635 ($\nu_{C=N}$), 1610, 1595 and 1585 cm^{-1} ($\nu_{C=C}$).

UV spectrum (methanol) λ_{max}: 256 nm (ε, 35,200).

IV.5 REFERENCES

1. G. W. Griffin and E. J. O'Connell, J. Am. Chem. Soc., 84, 4148 (1962).

2. H. E. Zimmerman, H. G. C. Dürr, R. G. Lewis and S. Bram, J. Am. Chem. Soc., 84, 4149 (1962).

3. A. Padwa, D. Crumrine and A. Shubber, J. Am. Chem. Soc., 88, 3064 (1966).

4. N. Sugiyama and C. Kashima, Bull. Chem. Soc. Japan, 43, 1875 (1970).

5. H. E. Zimmerman, H. G. C. Dürr, R. S. Givens and R. G. Lewis, J. Am. Chem. Soc., 89, 1863 (1967).

6. S. Lahiri, Ph.D. Thesis, Indian Institute of Technology, Kanpur, 1977

7. S. Lahiri, V. Dabral, S. M. S. Chauhan, E. Chakachery, C. Vijaya Kumar, J. C. Scaiano and M. V. George, J. Org. Chem., 45, 3782 (1980).

8. S. Lahiri, M. P. Mahajan, R. Prasad and M. V. George, Tetrahedron, 33, 3159 (1977).

9. R. E. Lutz, T. Amacker, S. M. King and N. H. Shearer, J. Org. Chem., 15, 181 (1950).

10. See, Chapter II of this thesis.

11. M. Gorodetsky and Y. Mazur, Tetrahedron Lett., 369 (1963).

12. M. Gorodetsky and Y. Mazur, J. Am. Chem. Soc., 86, 5213 (1964).

13. M. Gorodetsky and Y. Mazur, Tetrahedron, 22, 3607 (1966).

14. A. Yogev, M. Gorodetsky and Y. Mazur, J. Am. Chem. Soc., 86, 5208 (1964).

15. R. Huisgen, Angew. Chem. Internat. Ed. Engl., 19, 947 (1980).

16. R. E. Lutz and W. R. Smithey, J. Org. Chem., 16, 51 (1951).

17. C. S. Angadiyavar, Unpublished results.

VITAE

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